United States District Court,
D. Delaware.

SCHERING CORPORATION and Biogen, Inc,
Plaintiffs.
v.
AMGEN INC,
Defendant.

No. CIV.A. 96-587 MMS

Argued June 23, 1998.
Decided July 30, 1998.

Patentee and its licensee brought patent infringement suit against producer of consensus interferon product, alleging infringement of patent covering use of recombinant deoxyribonucleic acid (DNA) molecules in producing human interferon-like polypeptides. Producer of accused product counterclaimed, seeking declaratory judgment that patent was unenforceable, invalid, not infringed, and misused. The District Court, Murray M. Schwartz, Senior District Judge, construing patent claims, held that, among other things: (1) "IFN-(alpha)>>>" portion of the claim term "IFN-(alpha) type" referred to a single, naturally-occurring leukocyte interferon protein known at time of invention, which subsequently became referred to as IFN-(alpha)-1, and did not extend to other subspecies of interferon protein; (2) "IFN-(alpha) type" did not cover mature form of interferon protein; (3) references to DNA sequences which code on expression for a polypeptide of the IFN-(alpha) type, and DNA sequences which code on expression for a polypeptide of the IFN-(alpha) type coded for on expression by any of the foregoing DNA sequences and inserts, referred to both naturally occurring and non-naturally occurring DNA sequences which bore the genetic code for expressing the polypeptide but did not require actual expression and detection of the protein; and (4) phrase "substantially pure DNA sequence ... coding on expression for only a single polypeptide chain" referred to DNA sequence independent of any plasmid DNA in a host cell.

Ordered accordingly.

4,530,901. Cited.

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OPINION

MURRAY M. SCHWARTZ**, Senior District Judge.**

I. Introduction

Schering Corporation ("Schering") and Biogen, Inc. ("Biogen") (collectively "Schering") filed a patent infringement suit against Amgen, Inc. ("Amgen"), alleging Amgen infringed Biogen's U.S. Patent No. 4,530,901 ("the '901 Patent"), entitled "Recombinant DNA Molecules and Their Use in Producing Human Interferon-Like Polypeptides." FN1 Amgen answered the Complaint alleging various affirmative defenses and counterclaimed seeking a declaratory judgment that the '901 Patent is unenforceable, invalid, not infringed, and has been misused. Jurisdiction is proper under 28 U.S.C. s. 1338(a).

FN1. Biogen has granted to Schering an exclusive license in all fields to practice the '901 Patent. *See* Docket Item ("D.I.") 17 at para. 8, 9.

Pursuant to Markman v. Westview Instruments, Inc., 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996), the Court now construes the scope and meaning of disputed claim language in the '901 Patent.

II. Factual Background

A. History of Interferon

The '901 Patent relates generally to the synthesis of human alpha FN2 interferon (also referred to as "IFN-(alpha)"), a naturally occurring human protein that functions as an anti-viral and anti-tumor agent in human beings. FN3 The importance of interferon was first appreciated in the 1950s, and because of its ameliorative properties, became of interest as a pharmaceutical. Interferon may be produced by leukocyte cells (a type of white blood cell), fibroblast cells, or lymphoblastoid cells in the human body. The '901 Patent, however, addresses primarily leukocyte interferon which is produced in the human body when these cells are exposed to viruses or other foreign invaders. Only minute amounts of interferon, however, can be extracted from the human cells which produce it. As a result, researchers explored alternative ways interferon could be produced in mass quantities.

FN2. The three most common types of interferon are designated alpha, beta and gamma. This patent only deals with the alpha variety.

FN3. Interestingly, Schering decided to commercialize a subsequently cloned alpha interferon subtype, IFN-(alpha)-2, rather than the initially cloned interferon subtype, IFN-(alpha)-1. IFN-(alpha)-2 is sold as Intron A for the treatment of such diseases as hepatitis B, hepatitis C, and malignant melanoma. Part of the dispute between the parties relates to whether the '901 Patent covers both the IFN-(alpha)-1 and IFN-(alpha) >-2 subtypes.

The '901 Patent describes an alternative method by which to harvest alpha interferon: recombinant DNA FN4 technology.FN5 Briefly, the recombinant DNA technology at issue operates by: 1) identifying and isolating the DNA that contains the genetic code for manufacturing interferon in the human body; 2) inserting the isolated DNA into a bacterium which did not otherwise produce interferon; 3) growing the bacterium into enormous quantities, with each new bacterium containing the inserted interferon DNA; 4) utilizing the protein-making capacity of the bacteria cells to produce interferon; and 5) collecting the interferon from the bacteria to be used for pharmaceutical purposes.

FN4. DNA, or deoxyribonucleic acid, stores information about how a cell is to assemble various proteins. A complete set of the DNA genetic information is found in each cell of any given organism.

FN5. It is not necessary at this time to rehash in detail the fundamentals of molecular biology and recombinant DNA technology that undergird this invention. The Federal Circuit Court of Appeals sufficiently set out the fundamentals ten years ago in In re O'Farrell, 853 F.2d 894, 895-99 (Fed.Cir.1988). These basic principles still apply today. *See* Regents of the Univ. of Calif. v. Eli Lilly and Co., 119 F.3d 1559, 1562 n. 1 (Fed.Cir.1997); Kridl v. McCormick, 105 F.3d 1446, 1448 n. 1 (Fed.Cir.1997).

Dr. Charles Weissmann, the named inventor of the '901 Patent, was the first person able to identify and isolate DNA bearing the genetic code for human alpha interferon using recombinant DNA technology. Human leukocyte cells were induced to make interferon by exposing them to a virus. A RNA (ribonucleic acid) FN6 mixture was collected from the induced cells, which contained among its constituents RNA encoding for alpha interferon. Double-stranded DNA fragments (cDNA or copy DNA) corresponding to the RNA segments in this mixture were then made according to methods known in the art. These cDNA segments were spliced into plasmids (circular loops of DNA found only in bacteria) which were in turn inserted into E. coli bacteria. Thousands of these transformed bacteria were then grown into colonies of billions of bacteria, each of which contained a copy of the plasmid that transformed the bacteria.

FN6. Cells make proteins by transcribing DNA's genetic code onto a corresponding template called RNA. Thereafter, RNA is translated into a chain of amino acids called a protein.

Individual alpha interferon DNA was identified and isolated by systematically exposing the cDNA in the bacterial plasmid to the original RNA mixture. In this way, RNA complementary to the cDNA hybridized to the cDNA.FN7 The RNA, which hybridized to the cDNA, was then injected into frog oocytes (eggs) to determine if the RNA in question, when translated into protein, coded for interferon. Oocytes which contained the RNA coding for leukocyte interferon were effectively able to fight off viruses to which they were exposed, while the oocytes not coding for interferon died when exposed to the virus.

FN7. "Hybridization" refers to the association of complementary strands of RNA or DNA to form a double-stranded molecule of DNA-DNA, DNA-RNA, or RNA-RNA. The bond between paired nucleotides-A (adenine) with T (thymine) and C (cytosine) with G (guanine)-hold the double-stranded duplex together by means of hydrogen bonds. Taking advantage of the tendency of complementary DNA and RNA strands to hybridize, a molecular biologist may use a single strand of DNA or RNA to probe for structurally related DNA or RNA in a sample of many different strands of DNA and/or RNA.

In this general manner, the '901 Patent identifies a number of DNA sequences that code for alpha interferon ("the DNA inserts") which were each physically isolated by Dr. Weissmann. Each of these isolated DNA inserts, contained in a plasmid within a host cell, were then physically deposited with an official depository in Germany on January 7, 1980.FN8 The application for the '901 Patent was subsequently filed on February 4, 1980.FN9

FN8. Disclosure of biological material in a public depository effectively incorporates the deposited material, by reference, into the patent application. *See Ex Parte* Maizel, 27 U.S.P.Q.2d 1662, 1669, 1992 WL 519152 (Bd.Pat.App & Interf.1992).

FN9. Although the patent application was filed in February of 1980, because Schering deposited the DNA inserts on January 8, 1980, it claims priority back to that date. Thus, January 8, 1980 is effectively the filing date. *See* In re Lundak, 773 F.2d 1216, 1222-23 (Fed.Cir.1985).

Later, Dr. Weissmann made further discoveries, including the fact that there are a number of different genes that code for different subtypes of alpha interferon. As a result, Biogen, three months later, filed a continuation-in-part application to cover this newly discovered subject matter. However, a patent never issued on this continuation-in-part application.

B. The '901 Patent

The '901 Patent issued to Biogen on July 23, 1985, after being assigned to it by the inventor, Weissmann. Schering was subsequently granted an exclusive license to practice the '901 Patent.

[1] The independent claims of the '901 Patent, Claims 1, 5, 8, 9, and 12, are directed to: a substantially pure DNA sequence containing the DNA coding on expression for a polypeptide FN10 of the IFN-(alpha) type (Claim 8); a recombinant DNA molecule that may be used to express an IFN-(alpha) type polypeptide in a host cell (Claim 1); a host cell transformed with a recombinant DNA molecule containing DNA coding on expression for a polypeptide of the IFN-(alpha) type (Claim 5); and methods for producing these polypeptides involving: 1) the preparation of a recombinant DNA molecule containing an IFN-(alpha) type DNA sequence, 2) transformation of a host cell with the DNA molecule, 3) culturing of the host, and 4) collection of the IFN-(alpha) type protein product (Claims 9 and 12). Schering contends Amgen's consensus interferon product infringes all of these independent claims. FN11 Specifically, the following claim language is in dispute:

FN10. Polypeptides consist of a series of amino acids strung together by either covalent or non-covalent bonds known as peptide bonds. The term "polypeptide" and "protein" are not always synonymous. Although all proteins are polypeptides, not all polypeptides are proteins, i.e., chains of less than 50 amino acids are not proteins. *See* O'Farrell, 853 F.2d at 896 n. 3.

FN11. It is proper to keep the accused product in mind during the claim construction phase because it is efficient to focus on only those elements of the claim which are said to be infringed by the accused product. *See* Scripps Clinic & Research Foundation v. Genentech, Inc., 927 F.2d 1565, 1580 (Fed.Cir.1991). With

that thought in mind, Amgen's consensus interferon product is an "average" or "consensus" sequence such that most positions in the amino acid chain are occupied by amino acids that occurred at that position in the chain in all or most of the known naturally occurring alpha interferon subtypes. In October of 1997, the Food and Drug Administration ("FDA") approved the marketing of Amgen's consensus interferon product-sold under the brand name Infergen-for treatment of hepatitis C only.

1. "A recombinant DNA molecule consisting of segments of DNA from different genomes" (Claims 1, 5, 9 and 12);
2. "which have been joined end-to-end outside of living cells" (Claims 1, 5, 9 and 12);

3. "which have the capacity to infect some host and to be maintained therein, and the progeny thereof" (Claims 1, 5, 9 and 12);

4. "DNA sequences which hybridize to any of the foregoing DNA inserts," (Claims 1, 5, 8, 9, 12);

5. "A polypeptide of the IFN-(alpha) type," (Claims 1, 5, 8, 9, 12);

6. "(b) DNA sequences ... which code on expression for a polypeptide of the IFN-(alpha) type, and (c) DNA sequences which code on expression for a polypeptide of the IFN-(alpha) type coded for on expression by any of the foregoing DNA sequences ...." (Claims 1, 5, 8, 9, 12); and

7. "A substantially pure DNA sequence ... said DNA sequences coding on expression for only a single polypeptide chain," (Claim 8).

The Court, however, need only consider Claims 1 and 8, as they are representative of the claim disputes existing in the other independent claims. FN12 The disputed claim language will be construed according to the claim construction principles which are set out below.
FN12. Additionally, it is unnecessary to consider the dependent claims of the '901 Patent as a product that does not infringe an independent claim cannot infringe a dependent claim. *See* Eltech Sys. Corp. v. PPG Indus. Inc., 710 F.Supp. 622, 634 n. 10 (W.D.La.1988), *aff'd* 903 F.2d 805 (Fed.Cir.1990).

III. Applicable Law for Claim Construction

[2] Patent infringement actions consist of two discreet and separate phases. In the first phase, the Court construes the scope and meaning of a patent, while in the second phase, the claim, as properly construed, is compared to the accused product. *See* Gentry Gallery, Inc. v. Berkline Corp., 134 F.3d 1473, 1476 (Fed.Cir.1998). The first phase is known as claim construction and is exclusively a matter of law to be determined by the Court. *See* Cybor Corp. v. FAS Technologies, Inc., 138 F.3d 1448, 1455 (Fed.Cir.1998) (*in banc*). The Court only addresses the claim construction phase in this opinion.FN13

FN13. Amgen confuses the patent principle "a court [should] seek to interpret claims to preserve, rather than defeat, [patent] invalidity," *see* Eastman Kodak Co. v. The Goodyear Tire & Rubber Co., 114 F.3d 1547, 1555 (Fed.Cir.1997); *see also* Evans Medical Ltd. v. American Cyanamid Co., 1998 WL 312506 at (S.D.N.Y. June 10, 1998) ("It is a well-established rule of claim construction that claims should be interpreted, if possible, so as to preserve their validity.") (citing Amhil Enters. Ltd. v. Wawa, Inc., 81 F.3d

1554, 1561 (Fed.Cir.1996)), with permitting an out and out invalidity analysis during the claim construction phase of the litigation. This claim construction principle, however, was enunciated in the context of explaining why extrinsic evidence of the subjective intent of parties is disfavored. *See* Markman v. Westview Instr., Inc., 52 F.3d 967, 986 (Fed.Cir.1995), *aff'd,* 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996). Accused infringers were attempting to submit all types of extrinsic evidence, which if accepted by a court in its claim construction analysis, would render the claim invalid as construed. The Federal Circuit reasoned that if a patent's claim is sufficiently unambiguous for the PTO, it follows there should be no factual ambiguity which can only be resolved by resort to extrinsic evidence. *See* Markman, 52 F.3d at 986.

This salutary claim construction principle is a far cry from arguing that an indefiniteness or enablement analysis should always be performed during a claim construction. In fact, the Federal Circuit has explicitly stated that such invalidity arguments are clearly not a part of the claim construction analysis. *See* Intervet Am., Inc. v. Kee-Vet Labs., Inc., 887 F.2d 1050, 1053 (Fed.Cir.1989) ("Ambiguity, undue breadth, vagueness, and triviality are matters which go to claim *validity* for failure to comply with 35 U.S.C. s. 112, para. 2, not to interpretation or construction.") (emphasis in original). Accordingly, the Court declines to consider arguments of validity during the claim construction phase without more clear guidance from the Federal Circuit.

In addition, the Court only relies on extrinsic evidence for its construction of one disputed claim phrase. For all the other claim interpretations, it is not necessary to consider the enablement requirement under s. 112, para. 1 and interpret claim language narrowly so as to preserve its validity. *See* Digital Biometrics, Inc. v. Identix, Inc., 149 F.3d 1335, 1998 WL 394371 at *6-*7 (Fed.Cir. July 2, 1998) ("[I]f after consideration of the intrinsic evidence three remains a doubt as to the exact meaning of claim, consideration of extrinsic evidence may be necessary to determine the proper construction. If a claim falls into this latter category," questions of enablement under s. 112, para. 1 would support adoption of a narrower claim construction.) [3] Proper claim construction requires an examination of the claim language, the specification, and, if introduced, the prosecution history. FN14 *See* Phonometrics, Inc. v. Northern Telecom Inc., 133 F.3d 1459, 1464 (Fed.Cir.1998) (citing Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996)). Foremost in importance is the asserted claim itself and, therefore, the claim language constitutes the appropriate starting point for the claim construction analysis. *See id.* (citations omitted); *see also* Vitronics, 90 F.3d at 1582 (a court "must look to the words of the claims themselves, both asserted and nonasserted, to define the scope of the patented invention.").

FN14. Schering advances the proposition that if a patent is a "pioneer patent," i.e., a distinct step in the progress of the art, *see* Westinghouse v. Boyden Power-Brake Co., 170 U.S. 537, 562, 18 S.Ct. 707, 42 L.Ed. 1136 (1898), it should be accorded a "judicially 'liberal' view [for] both claim interpretation and equivalency." *See* Texas Instruments, Inc. v. U.S. Int'l Trade Comm., 846 F.2d 1369, 1370 (Fed.Cir.1988). However, Schering has cited the Federal Circuit Court of Appeals out of context. The passage continues by stating: "However, even its 'pioneer' status does not change the way infringement is determined. The patentee's disclosure, the prosecution history, and the prior art still provide the background against which the scope of claims is determined." Whether a means-plus-function clause under a s. 112, para. 6 equivalency determination may be affected by the pioneer status of an invention is a question of some disagreement in the Federal Circuit Court of Appeals and need not be decided by the Court at this time. *Compare* Intel Corp. v. U.S. Int'l Trade Comm., 946 F.2d 821, 842 (Fed.Cir.1991) (pioneer status not important in structural equivalency determination under 35 U.S.C. s. 112, para. 6) *with* Texas Instruments v. U.S. Int'l Trade Comm., 805 F.2d 1558, 1569-71 (Fed.Cir.1986) (pioneer status relevant to means-plus-

function equivalency determination). Suffice it to say, claim language, not governed by 35 U.S.C. s. 112, para. 6, is governed by the same claim construction principles irrespective of pioneer status.

[4] [5] [6] [7] Particularly significant in this case is the principle that claim language is interpreted to ascertain the meaning that a person of ordinary skill in the art would give to the claims in dispute. *See* Wiener v. NEC Electronics, Inc., 102 F.3d 534, 539 (Fed.Cir.1996). The operative time for determining what meaning the disputed language of the claim has in the art is the date of the application for the patent.FN15 *See id*. While disputed claim language will normally be given its ordinary and customary meaning, "a patentee may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition is clearly stated in the patent specification or file history." Vitronics, 90 F.3d at 1582. Further, claims in the same patent are to be interpreted with reference to one another. *See* Southwall Technologies, Inc. v. Cardinal IG Co., 54 F.3d 1570, 1579 (Fed.Cir.), *cert. denied,* 516 U.S. 987, 116 S.Ct. 515, 133 L.Ed.2d 424 (1995).

FN15. Schering thus incorrectly relies on definitions and descriptions found in patents that issued well after the '901 Patent application was filed. Regardless, these latter-issued patents represent extrinsic evidence which is disfavored during claim construction analysis.

[8] [9] [10] If the scope and the meaning of the claim language is ambiguous, the Court next considers the specification, which may be examined to more properly understand the metes and bounds of the claim. *See* Vitronics, 90 F.3d at 1582. The specification acts as a dictionary when it either expressly, or by implication, defines terms used in the claims. *See id*. As a result, the specification has been described as "often the single best guide to the meaning of a disputed term ...." *See id*. When the specification explains and defines a term used in the claims, without ambiguity or incompleteness, there is no need to search further for the meaning of the term. *See* Multiform Desiccants, Inc. v. Medzam, Ltd., 133 F.3d 1473, 1478 (Fed.Cir.1998). The specification, however, cannot be used to import language into the claim limitation in a wholesale fashion. Although, "examples disclosed in the preferred embodiment may aid in the proper interpretation of a claim term, the scope of a claim is not necessarily limited by such examples." Ekchian v. Home Depot, Inc., 104 F.3d 1299, 1303 (Fed.Cir.1997); Intervet Am., 887 F.2d at 1053 ("[I]nterpreting what is meant by a word in a claim is not to be confused with adding an extraneous limitation appearing in the specification, which is improper.").

[11] [12] When the prosecution history is introduced into evidence, it informs the understanding of terms found in both the specification and the claim. *See* Multiform Desiccants, 133 F.3d at 1478 ("The evolution of restrictions in the claims, in the course of examination in the [Patent and Trademark Office], reveals how those closest to the patenting process-the inventor and the patent examiner-viewed the subject matter."). Indeed, the prosecution history may limit, through prosecution history estoppel, the interpretation of the disputed language to meanings not expressly disclaimed by the inventor during the prosecution of the patents. *See* CVI/Beta Ventures, Inc. v. Tura LP, 112 F.3d 1146, 1152 (Fed.Cir.1997) (quoting Southwall, 54 F.3d at 1579), *cert. denied sub nom*. Marchon Eyewear v. Tura LP, 522U.S. 1109, 118 S.Ct. 1039, 140 L.Ed.2d 105 (1998). Additionally, the prosecution history cannot enlarge, diminish or vary the limitations in the claims. *See* Markman, 52 F.3d at 980.

[13] [14] [15] "[I]f necessary to aid the court's understanding of the patent," the Court may consider extrinsic evidence. *See* Wright Medical Technology, Inc. v. Osteonics Corp., 122 F.3d 1440, 1443

(Fed.Cir.1997). Technical treatises and dictionaries are favored over other forms of extrinsic evidence. *See* Vitronics, 90 F.3d at 1584 n. 6.FN16 If, however, the intrinsic evidence unequivocally describes the meaning and scope of the disputed language, reliance on any extrinsic evidence is improper. *See* id. at 1583; Bell & Howell Document Management Products Co. v. Altek Systems, 132 F.3d 701, 705 (Fed.Cir.1997) ("The intrinsic evidence should usually be sufficient to enable one to determine the meaning of a claim term."). As a result, the testimony of an inventor or his attorney concerning claim construction is entitled to little or no consideration. *See* Bell & Howell, 132 F.3d at 706.

FN16. Technical treatises and dictionaries may not be employed, however, to contradict anything in the patent documents. *See* Vitronics, 90 F.3d at 1584 n. 6.

[16] Lastly, the Court is not limited to picking between definitions supplied by the parties. The Federal Circuit has stated in this context:

It may well be that often in some cases one side or the other will offer the correct claim interpretation to the judge. More often, however, it is likely that the adversaries will offer claim interpretations arguably consistent with the claims, the specification and the prosecution history that produce victory for their side. In any event, the judge's task is not to decide which of the adversaries is correct. Instead the judge must independently assess the claims, the specification, and if necessary the prosecution history, and relevant extrinsic evidence, and declare the meaning of the claims.

Exxon Chemical Patents, Inc. v. Lubrizol, Corp., 64 F.3d 1553, 1556 (Fed.Cir.1995). Specifically, as to declarations submitted by diametrically opposed experts, the Court expressly does not make factual findings or choose between them. The experts only inform the Court regarding their respective view on how the law should be interpreted.

These claim construction principles will now be applied to the disputed claim language in the '901 Patent.

IV. Claim Construction of the '901 Patent

A. Claim 1

The language in dispute in Claim 1 FN17 can be more easily analyzed if subdivided into six distinct phrases: 1) "recombinant DNA molecule consisting of segments of DNA from different genomes," 2) "joined end-to-end outside of the living cells," 3) "capacity to infect some host and to be maintained therein, and the progeny thereof," 4) "DNA sequences which hybridize to any of the foregoing DNA inserts," 5) "a polypeptide of the IFN-(alpha) type," and 6) "DNA sequences ... which code on expression for a polypeptide of the IFN-(alpha) type, and DNA sequences which code on expression for a polypeptide of the IFN-(alpha) type coded for on expression by any of the foregoing DNA sequences and inserts." Each of these claim phrases will be examined in turn.

FN17. Claim 1 of the '901 Patent reads:
1. A recombinant DNA molecule consisting of segments of DNA from different genomes which have been joined end-to-end outside of living cells and which have the capacity to infect some host and to be maintained therein, and the progeny thereof, comprising a DNA sequence selected from the group consisting of: (a) the DNA inserts of Z-pBR322(Pst)/HcIF-2h (DSM 1700), Z-pBR322(Pst)/HcIF-SN35 (DSM 1701), Z-pBR322(Pst)/HcIF-SN42 (DSM 1702) and ZpKT287(Pst)/HcIF-2h-AH6 (DSM 1703), (b)

DNA sequences which hybridize to any of the foregoing DNA inserts and which code on expression for a polypeptide of the IFN-(alpha) type, and (c) DNA sequences which code on expression for a polypeptide of the IFN-(alpha) type coded for on expression by any of the foregoing DNA sequences and inserts, said DNA sequences and inserts being operatively linked to an expression control sequence in said recombinant DNA molecule.

Col. 36, lines 4-24.

1. "recombinant DNA molecule consisting of segments of DNA from different genomes"

This claim language can be more efficaciously explored by further dividing it into three smaller segments: a) "recombinant DNA molecule," b) "consisting of," and c) "segments of DNA from different genomes."

a. "recombinant DNA molecule"

[17] There is not, and there could not be, any dispute about the meaning of this term as it is specifically defined in the specification:

Recombinant DNA Molecule or Hybrid DNA-A molecule consisting of segments of DNA from different genomes which have been joined end-to-end outside of living cells and the have the capacity to infect some host cell and being maintained therein.

See Col. 7, lines 33-37. When the specification is acting as a dictionary, expressly defining a term used in the claims, it is "the single best guide to the meaning of the disputed term ...." *See* Vitronics, 90 F.3d at 1582. Accordingly, the Court adopts this definition for "recombinant DNA molecule." Unfortunately, however, this definition is singularly unhelpful because it merely mimics the language in the claim that follows the term "recombinant DNA molecule." Thus, it is necessary to construe the ensuing claim terms to gain an insight into the scope and meaning of this claim element.

b. "consisting of"

[18] Amgen argues "consisting of," a term of art in patents, excludes the presence of non-recited elements. Schering counters that "consisting of" is not used as a "transitional phrase," but is part of Claim 1's "preamble," and thus, there is no need to afford it its special patent law meaning.

[19] [20] In patent law, there are terms whose meaning cannot be changed by individual parties. Two such phrases are "consisting of" and "comprising." *See* In re Gray, 19 C.C.P.A. 745, 53 F.2d 520, 521 (CCPA 1931). "Comprising" indicates the claim is open and additional elements not recited can be covered by the claim, whereas "consisting of" indicates the claim is closed and no elements not recited may be included in the claim's definition. *See id.;* Mannesmann Demag Corp. v. Engineered Metal Products Co., 605 F.Supp. 1362, 1379 (D.Del.1985), *aff'd,* 793 F.2d 1279 (Fed.Cir.1986); D. Chisum, 2 Patents s. 8.06[1][b] at 8-99 to 8-102 (1984). However, in deciding whether to apply these "special meanings" in construing a claim, one must first ask whether a special clause such as "consisting of" is part of the preamble, body or transition of the patent.FN18 *See* Regents of Univ. of Calif. v. Eli Lilly & Co., 39 U.S.P.Q.2d 1225, 1258 n. 15, 1995 WL 735547 (S.D.Ind.1995), *aff'd in pertinent part,* 119 F.3d 1559 (Fed.Cir.1997), *cert. denied,* 523 U.S. 1089, 118 S.Ct. 1548, 140 L.Ed.2d 695 (1998); *Chisum* at s. 8.06[1][b] at 8-99 (1998). Only if "consisting of" is part of the transitional section of the claim will it be afforded the "special" limited meaning enunciated above. *See* Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 1271-72 & n. 8 (Fed.Cir.1986)

(construing "comprising").

FN18. The preamble sets the stage for the recitations which follow, either by summarizing the invention expressed by the claims and/or placing it in the perspective of the prior art. Peter Rosenberg, *Patent Law Fundamentals* s. 14.05[1] at 14-21 (Rev. Ed.1998). The transitional phrase is the introductory clause between the preamble and the limitations of a claim, and materially affects the scope of protection afforded by the claim language. *Id*. at s. 14.05[2] at 14-28. The body of the claim, which is all the language coming after the transitional phrase, states, as a series of phrases, the structural elements which make up and form the nucleus of the invention. *Id*. at s. 14.05[3] at 14-32.

In the '901 Patent, "consisting of" in the disputed claim language is employed in the following manner:

1. A recombinant DNA molecule *consisting of* segments of DNA from different genomes which have been joined end-to-end outside of living cells and which have the capacity to infect some host and to be maintained therein, and the progeny thereof, comprising a DNA sequence selected from the group *consisting of:*

(a) the DNA inserts ....

(b) DNA sequences which hybridize ....

(c) DNA sequences which code on expression ....

See Col. 36, lines 4-5, 8-17 (emphasis added). After analyzing the pertinent language of this claim, the Court finds the first mention of "consisting of" is clearly utilized as a transitional phrase in the claim, i.e., all the language coming after "consisting," states, as a series of phrases, the structural elements which make up and form the nucleus of the invention. *See* Rosenberg s. 14.05[3] at 14-32. Further, the term "recombinant DNA molecule" coming before this "consisting of" language is not properly a one word preamble summarizing the invention expressed by the claims. *See id*., s. 14.05[1] at 14-21. The fact that the second "consisting of" phrase is also a transition phrase is inconsequential as neither the Court nor the parties have been able to point to a case which stands for the proposition that there cannot be two transitional phrases in one claim. Ergo, the "special meaning" ascribed to "consisting of" when found in a transitional phase is appropriately applied to the first "consisting of" phrase found in the claim language. The Court therefore finds "consisting of" in Claim 1, Col. 36, line 4, indicates the claim is closed and no elements not recited in the claim may be included.

c. "segments of DNA from different genomes"

[21] The crux of the dispute concerning this claim language, and which underlies many of the ensuing claim disputes between the parties, is whether the DNA segments that form the recombinant DNA molecule have to be from naturally-occurring genomes or may also be from non-naturally occurring genomes. Amgen argues this phrase must be construed narrowly such that the segments of DNA that make up the recombinant DNA molecule must be taken from the DNA of different naturally-occurring cells or viruses, e.g., segments of DNA from human beings and bacteria. Schering, on the other hand, maintains that the term "genome" should be interpreted broadly to mean the recombinant DNA molecules may be taken from both naturally occurring DNA sequences and from non-naturally occurring DNA sequences, such as those DNA sequences

found in the engineered plasmids described in the specification.

The term "genome" is defined in the specification:

Genome-The entire DNA of a cell or a virus. It includes inter alia the structural genes coding for the polypeptides of the substance, as well as operator, promoter and ribosome binding and interaction sequences, including sequences such as the Shine-Dalgarno sequences.

See Col. 6, lines 57-62. It is unclear from this definition whether a genome is limited to DNA that originated in nature. Schering argues that the recombinant DNA molecules described in the '901 Patent specification include DNA sequences that did not originate in nature; specifically, the pBR322 and pKT287 engineered plasmids that were used as cloning vehicles. *See* Col 27, lines 8-27; Col. 30, line 42. Because Schering asserts it is well-settled patent law that claims should be interpreted to encompass the embodiments of the specification, *see* Vitronics, 90 F.3d at 1583, it contends this claim language must be construed to include the engineered plasmids which did not originally occur in nature. Further, Schering finds support in the specification which states:

A wide variety of host/cloning vehicle combinations may be employed in cloning the double stranded cDNA prepared in accordance with this invention. For example, useful cloning vehicles may consist of segments of chromosomal, non-chromosomal and synthetic DNA sequences, such as ... vectors derived from combinations of plasmids and phage DNAs such as plasmids which have been modified.

See Col. 12, lines 3-14.

The Court agrees with Schering that the examples disclosed in the specification take DNA segments from the genome of both naturally occurring and non-naturally occurring cells. Not only does a recombinant DNA molecule's genome not occur in nature, but at least one of the segments of DNA that make up this recombinant molecule may not come from nature. Specifically, the recombinant DNA molecules synthesized in the specification include either the pBR322 or pKT287 bacterial plasmids, which both parties agree, were engineered in the laboratory. *See also* D.I. 186 at 3, 6. Amgen argues, however, that even though the plasmid product is engineered in the laboratory, the plasmids consist of natural DNA, with the exception of one synthetic nucleotide in pKT287.

Significantly, it is the bacterial genome as a whole, which is not naturally-occurring, and the desired interferon-type DNA sequence which are spliced together to form the recombinant DNA molecule. *See* Col. 36, lines 4-5. The combination of natural DNA with other non-natural constituents to form the pKT287 and pBR322 plasmids is not part of the '901 invention, but existed previously in the art. *See* Col. 13, lines 61-68 (pBR322); Col. 30, lines 42-43 (pKT287). Accordingly, regardless of whether the patent permits the splicing together of more than two segments of DNA from different genomes, as Amgen urges, the fact of the matter is that the preferred embodiment contemplates splicing an alpha interferon type segment with an engineered plasmid. The preferred embodiment must be covered by any interpretation of this claim language as an interpretation of a claim term which excludes a preferred embodiment is to be avoided. *See* Vitronics, 90 F.3d at 1582. The Court thus construes "segments of DNA from different genome" as permitting segments of DNA from genome of both naturally occurring cells or viruses and non-naturally occurring cells and viruses.

[22] [23] The prosecution history further strengthens this conclusion. Under the doctrine of prosecution

history estoppel, the prosecution history may limit the interpretation of the disputed language to meanings not expressly disclaimed by the inventor during the prosecution of the patents. *See* CVI/Beta Ventures, 112 F.3d at 1155 (quoting Southwall, 54 F.3d at 1579). This estoppel "may arise either from matters surrendered as a result of amendments to overcome patentability rejections ... or as a result of argument to secure allowance of a claim." *See* Cybor, 138 F.3d at 1460. However, the reason for offering an amendment or an argument remains relevant to the application of an estoppel. *See* Litton Systems, Inc. v. Honeywell, Inc., 140 F.3d 1449, 1456 (Fed.Cir.1998). It is thus important for the Court to determine the reason a patentee submitted an argument or amendment during the prosecution of the patent. *See* Warner-Jenkinson Co. v. Hilton Davis Chem. Co., 520 U.S. 17, 117 S.Ct. 1040, 1051, 137 L.Ed.2d 146 (1997).

The originally filed claims recited: "DNA from whatever source obtained, including natural, synthetic, or semi-synthetic sources, related by mutation, including single or multiple, base substitutions, deletions, insertions, and inversions to any of the foregoing DNA sequences or inserts." D.I. 172, Tab 1 at 64 (February 4, 1980). Amgen argues that because Biogen was forced to eliminate this language by the patent examiner, Biogen is now estopped from claiming synthetic and semi-synthetic sources for the DNA segments from different genomes. In rejecting this initial claim language, however, the examiner found over broad the use of the terms "related by mutation," "multiple base substitutions," "deletions," "insertions," and "inversions," but significantly did not question the validity of the terms "synthetic" or "semi-synthetic." *See id.,* Tab 17 at 3 (November 29, 1982). Accordingly, the Court finds prosecution history estoppel does not bar an interpretation of "segments of DNA from different genomes" which includes both naturally occurring and non-naturally occurring DNA segments.FN19

FN19. Amgen points to another part of the prosecution history in which Biogen explained the use of human and bacterial DNA:
As defined in the art and in this application, a recombinant DNA molecule consists of segments of DNA from different genomes (the entire DNA of a cell or virus) .... The specific recombinant DNA molecules of claims 1-9 consist of particular DNA that codes for human leukocyte interferon ... joined end-to-end with a segment of DNA from another genome [e.g., *E. coli*]. It could not be plainer that such a combination is not naturally occurring.

D.I. 172, Tab 11 at 7 (January 27, 1982). Amgen infers from this statement that although the resulting combination of two genomes is not itself naturally occurring, the individual constituents must be naturally occurring. The Court is not persuaded. Prosecution history may only inform the Court's understanding of the specification and the claim, it cannot add limitations to a claim that directly contradict a preferred embodiment. *See* Markman, 52 F.3d at 980. Therefore, the Court declines to make such an inference from this prosecution history language.
For all of these reasons, the Court holds the claim language "segments of DNA from different genomes" refer to DNA segments or DNA sequences in genomes of cells or viruses which may be both naturally occurring and non-naturally occurring. Combining the above construed elements, the Court finds the claim language "[a] recombinant DNA molecule consisting of segments of DNA from different genomes" refers to a molecule which may consist of segments of DNA in genomes from both naturally occurring or non-naturally occurring cells or viruses.

2. "joined end-to-end outside of the living cells"

[24] The dispute concerning this claim language is whether this phrase is a product-by-process claim.

Amgen argues it is and therefore, this claim language is a process limitation that requires the joinder of DNA end-to-end outside of the living cell. Schering disagrees. It asserts this language is not in product-by-process form. Instead, Schering argues that it is only a structural limitation as to the term "recombinant DNA molecule," and therefore, this claim language may encompass an identical product made by a different process.

[25] "Product-by-process claims" are claims which describe the product more by the process used to obtain it than by its structure. *See* Hazani v. United States Int'l Trade Comm., 126 F.3d 1473, 1479 (Fed.Cir.1997). Although not referred to in the patent statute, product-by-process claims developed in response "to the need to enable an applicant to claim an otherwise patentable product that resists definition other than by the process by which it is made." *See* In re Thorpe, 777 F.2d 695, 697 (Fed.Cir.1985).

The Court, however, is not persuaded that the phrase "joined end-to-end outside of living cells" is in product-by-process form. Product-by-process claims recite how a product is made, not how it is used. *See* Mentor Corp. v. Coloplast, Inc., 998 F.2d 992, 997 (Fed.Cir.1993). This claim language, however, is best characterized as a pure product claim since the product is described by its structure rather than by the process used to obtain it. *See* Hazani, 126 F.3d at 1479. Accordingly, the Court finds "joined end-to-end outside of living cells" to be a structural limitation which may encompass identical products made by different processes.

3. "capacity to infect some host and to be maintained therein, and the progeny thereof"

[26] Amgen contends this language requires that the joined segments of DNA must not only be able to infect a host cell and be maintained therein but also these same DNA segments must not be lost by its progeny. Schering retorts that Amgen has misconstrued this phrase by not properly applying the comma in the phrase, which would actually make two separate phrases of the claim language. As a result, Schering argues this claim language does not require the desired DNA segments to be maintained by the progeny of the initial host cells.

The Court is persuaded that the comma does not act to distinguish between two separatephrases. As stated previously, Claim 1 reads in pertinent part:

A recombinant DNA molecule consisting of segments of DNA from different genomes which have been joined end-to-end outside of living cells and which have the capacity to infect some host and to be maintained therein, and the progeny thereof ....

See Col. 36, lines 4-8. Reading this claim language as a coherent whole, the claim language does require that the recombinant DNA molecules infect the progeny of the host, but does not require the recombinant DNA molecules be maintained in the progeny. If the claim language was to be construed otherwise, the sentence would have been written in the following manner: "... which have the capacity to infect some host *and its progeny* and be maintained therein ...." Instead, the claim language merely reflects that the patentee wishes not only to cover the first generation of host cells that were infected by the recombinant DNA molecule but also the progeny which result from the reproduction of the host cells. While the purpose is not readily apparent, the claim language, as written, also takes into account the instance where even if the recombinant DNA molecule infects the progeny of the host, there is still a chance the recombinant DNA molecules may not be maintained in the progeny. As such, the Court finds "which have the capacity to infect some host and to be maintained therein, and the progeny thereof," requires that the recombinant DNA

segments infect the progeny of the host cells, but not necessarily to be maintained therein.

4. "DNA sequences which hybridize to any of the foregoing DNA inserts"

This claim language contains two distinct claim terms which must be analyzed: a) "DNA inserts" and b) "hybridize." The Court will consider each of these claim terms in turn.

a. "DNA Inserts"

[27] Both parties agree that the "DNA inserts" refer to the inserts contained within the E. coli bacterial cells deposited with the Deutsche Sammlung von Mikroorganismen ("DSM") in Germany. Amgen further seeks to establish that: 1) the inserts refer to the discrete sequences that are released from the deposited plasmids by using a restriction enzyme to cut the DNA insert and 2) the inserts are all derived from the same interferon gene. Schering asserts these added limitations are not part of the definition of "DNA inserts" and it is improper to read such limitations into the claim terms from the examples in the specification and from deposition testimony.

The Court agrees with the parties that the DNA inserts are clearly set out in the '901 Patent. Claim 1 reads in pertinent part:

A recombinant DNA molecule ... comprising a DNA sequence selected from the group consisting of:

(a) the DNA inserts of [Z-pBR322(Pst)/HcIF-4c (DSM 1699,] FN20 Z-pBR322(Pst)/HcIF-2h (DSM 1700), Z-pBR322 (Pst)/HcIF-SN35 (DSM 1701), Z-pBR322(Pst)/HcIF-Sn42 (DSM 1702) and ZpKT287(Pst)/HcIF-2h-AH6 (DSM 1703),

FN20. The DSM 1699 DNA insert only appears in claims 5 and 8. Schering was unable at oral argument to explain this difference in the claims.

(b) DNA sequences which hybridize to any of the foregoing DNA inserts ....
Col. 36, lines 4-15. Although the DNA inserts described include the designation "(Pst)" to refer to the restriction site where the plasmid was cut, FN21 the claim language limits what is claimed to the "DNA inserts" of the recombinant DNA molecule. Importantly, the restriction enzyme, the plasmid, and the bacterial host in which the isolated DNA sequences are found, are not part of the '901 invention.
FN21. The letters and number before the (Pst) designation refer to the plasmid being utilized from the E. coli bacteria, i.e., pBR322. The "Z-" designation before the plasmid refers to the fact that the plasmid was derived in Zurich, Switzerland. The letters and numbers after the slash ("/") refer to the DNA inserted into the plasmid, i.e., HcIF-2. Finally, the DSM number is the designation given to the organism by the public depository in Germany.

Further, there is no hint in either the claim or the specification that the DNA inserts are, or must be, derived from the same interferon gene. Although this might have turned out to be the case, as illustrated by subsequent deposition testimony, such information was not known to anyone at the time the patent application was filed in January of 1980. Because the Court must construe claim language according to the meaning a person of ordinary skill in the art would ascribe to it at the time of the patent application, *see* Wiener, 102 F.3d at 539, it cannot conclude as part of the "DNA insert" definition that all DNA inserts had

to be derived from the same interferon gene, as such knowledge was lacking in the relevant scientific community at the time of the '901 Patent application. The Court therefore finds that the claim term "DNA inserts" refers to those DNA inserts deposited at the DSM and explicitly set out in the claim language of the '901 Patent.

b. "hybridize"

[28] Both parties agree that hybridization includes the process by which one strand of DNA or RNA binds and forms a double-stranded structure with a complementary strand of RNA or DNA. *See supra* note 7. Specifically, hybridization was used in this invention to identify DNA segments structurally similar to both RNA segments and DNA segments found to code on expression for proteins with the anti-viral characteristics of interferon. The parties also agree that hybridization between two complementary strands is affected by such factors as time of exposure, temperature, salt concentration, and the degree of homology (amount of complementary nucleotides) between the two segments. Although the parties do not dispute that the selection of hybridization conditions is critical to the performance of the hybridization, the parties cannot agree what specific hybridization conditions are required by the claim. Schering argues that the conditions must be as stringent or more stringent than the conditions used by Dr. Weissmann in performing the hybridizations described in the patent specification.FN22 Amgen, on the other hand, contends the particular hybridization conditions disclosed in the specification must be used.

FN22. Conditions may be as stringent as those described in the specification, without being the exact same conditions, by varying the variables involved in the hybridization, e.g., the salt concentration and the temperature, in such a manner as to produce equivalent or more stringent hybridization conditions.

[29] Starting with the language of the patent itself, "hybridize" is not defined in the claim, nor is it defined in the specification. Specific conditions for the hybridization, however, are recited in the specification, *see* Col. 26, line 28 through Col. 27, line 2. Nevertheless, it is improper claim construction to import specification language into the claims. *See* Intervet Am., 887 F.2d at 1053. While claims are to be interpreted in light of the specification, it does not follow that extraneous limitations from the specification may be read into the claims. *See* CVI/Beta Ventures, 112 F.3d at 1158 (citing Sjolund v. Musland, 847 F.2d 1573, 1581 (Fed.Cir.1988)). As a result, the Court cannot agree with Amgen that the particular hybridization conditions disclosed in the specification are all that is covered by the '901 Patent.FN23

FN23. Regardless, the specification does not support Amgen's 87% homology figure for DNA-DNA hybridizations as that figure only applies to DNA-RNA hybridizations, which was performed at a different stage of the invention. *See* Col. 19, lines 7-13. Significantly, no minimum homology figure is established for DNA-DNA hybridizations. *See* Col. 26, lines 28-67.

[30] Although the specification may not be properly used to add extraneous limitations to a claim, a limitation is not extraneous when there is a need to interpret what the patentee meant by a particular ambiguous word or phrase in the claim. *See* E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co., 849 F.2d 1430, 1433 (Fed.Cir.), *cert. denied,* 488 U.S. 986, 109 S.Ct. 542, 102 L.Ed.2d 572 (1988). Such is the case here because both parties agree that the selection of hybridization conditions, such as time, temperature, salt concentration, and structural homology, is essential to the performance of the hybridization and to the overall invention. As the specification is the single best guide to the meaning and scope of the claims, *see*

Vitronics, 90 F.3d at 1582, the Court therefore finds the claim term "hybridize" necessarily includes conditions at least as stringent as those set forth in the specification.Additionally, as more stringent conditions necessarily subsume less stringent hybridization conditions, such conditions are also properly within the patent. The Court therefore holds the claim language "DNA sequences which hybridize to" refers to hybridization of other DNA to DNA inserts deposited at the DSM, under conditions as stringent or more stringent than those that exist in the specification.

Accordingly, combining the above two constructed phrases, the claim language "DNA sequences which hybridize to any of the foregoing DNA inserts" refers to DNA segments, which under conditions as least as stringent as those set forth in the specification of the '901 Patent, are able to bind and form a double-stranded structure with those DNA inserts specified in the patent and deposited at the DSM.

5. "a polypeptide of the IFN-(alpha) type"

Much paper has been devoted to this claim interpretation dispute. Unhappily, the Court will be no different. The language may be parsed into two queries: a) whether the "IFN-(alpha)" portion of the claim term "IFN-(alpha) type" refers to a single protein or multiple interferon proteins and b) whether the entire claim language, i.e, "IFN-(alpha) type," may refer to a mature interferon protein.

a. Number of Interferon Subspecies To Which "IFN-(alpha)" Refers

[31] Schering asserts that it is "self-evident" that the claim language "IFN-(alpha) type" contains two related claim terms: "IFN-(alpha)" and "IFN-(alpha) type." The term "IFN-(alpha)," Schering submits, refers to proteins which have the same amino acid sequences as the amino acid sequence of the naturally occurring IFN-(alpha) proteins. As a consequence, Schering argues that "IFN-(alpha)" refers to all the sub-species of IFN-(alpha). Schering points out that although originally referred to as "leukocyte interferon" in the patent, leukocyte interferon was later changed in the patent to "IFN(alpha)" to reflect a nomenclature change in the art adopted shortly after the patent was filed. Schering distinguishes "IFN-(alpha) type," to mean DNA encoding IFN-(alpha) that may have adjacent to it DNA encoding additional amino acids, such as leaders, tails (linkers), or fusion partners.

[32] [33] Amgen disagrees with Schering on almost every one of the above points. As an initial point, Amgen contends that "IFN-(alpha) type" is indefinite. Recognizing that the Court was unlikely to make a validity finding during claim construction, Amgen does agree that "IFN-(alpha) type" refers to DNA encoding both IFN-(alpha) and additional adjacent amino acids. Nevertheless, Amgen argues that polypeptides of "IFN-(alpha) type" must, not may, refer to DNA encoding for IFN-(alpha) and additional, adjacent amino acids. This is because Amgen asserts "IFN-(alpha) type" does not also include within it the term "IFN-(alpha)." Amgen also vehemently contests the that this claim language covers all the subspecies of alpha interferon, most of which were not known at the time of the invention.FN24

FN24. Amgen also urges the Court take into account a consent judgment and settlement recently entered into between Schering and Genentech in the United States District Court for the District of Massachusetts. *See Biogen v. Genentech,* C.A. No. 96-10862-MEL (D.Mass.1998), D.I. 181, Ex. V. However, such evidence is clearly extrinsic and may not come into evidence unless the intrinsic evidence of the record is ambiguous. *See* Bell & Howell, 132 F.3d at 705. Although some ambiguity is found to exist, the Court declines to consider the Massachusetts consent judgment, favoring reliance on a "favored" type of extrinsic evidence, a technical treatise, to resolve the ambiguity. *See* Vitronics, 90 F.3d at 1584 n. 6.

Nor is the Court bound by issue preclusion to take account of the Massachusetts litigation as a matter of law as Amgen suggests. Under issue preclusion, formerly known as collateral estoppel, "once a court has decided an issue of fact or law necessary to its judgment, that decision may preclude relitigation of the issue in a suit on a different cause of action involving a party to the first case." Allen v. McCurry, 449 U.S. 90, 94, 101 S.Ct. 411, 66 L.Ed.2d 308 (1980) (citing Montana v. United States, 440 U.S. 147, 153, 99 S.Ct. 970, 59 L.Ed.2d 210 (1979)). The Supreme Court has stated that "a litigant who was not a party to a federal case [may] use collateral estoppel 'offensively' in a new federal suit against the party who lost on the decided issue in the first case." *Id*. (citing Parklane Hosiery Co. v. Shore, 439 U.S. 322, 329-30, 99 S.Ct. 645, 58 L.Ed.2d 552 (1979)). "But one general limitation the [Supreme] Court has repeatedly recognized is that the concept of collateral estoppel cannot apply when the party against whom the earlier decision is asserted did not have a 'full and fair opportunity' to litigate that issue in the earlier case." *Id*. (citing Montana, 440 U.S. at 153, 99 S.Ct. 970; Blonder-Tongue Laboratories, Inc. v. University of Illinois Foundation, 402 U.S. 313, 328-329, 91 S.Ct. 1434, 28 L.Ed.2d 788 (1971)).

In this instance, Schering did not have a full and fair opportunity to litigate the construction to be given to the '901 Patent claim language and thus, issue preclusion does not properly apply. In fact, the Massachusetts consent judgment only involves an interference between Schering and Genentech concerning the continuation-in-part application filed in April of 1980. Regardless, the Court is not bound to accept the definition supplied, or admitted to, by either party. *See* Exxon Chemical Patents, 64 F.3d at 1556 ("[T]he judge's task is not to decide which of the adversaries is correct. Instead the judge must independently assess the claims, the specification, and if necessary the prosecution history, and relevant extrinsic evidence, and declare the meaning of the claims."). For all these reasons, then, the Court declines to consider the consent judgment Schering entered into with Genentech in Massachusetts.
[34] Difficulty in analyzing this claim language stems from the fact that the language, "a polypeptide of the IFN-(alpha) type," was not added to the claim of the '901 Patent until after the patent application had been submitted and in fact, "IFN-(alpha) type" appears nowhere in the specification. Indeed, the nomenclature upon which "IFN-(alpha) type" is based was not developed until six months after the patent application was filed. *See* Col. 1, lines 21-23 ("In this application the interferon nomenclature announced in *Nature* 286, p.110 (July 10, 1980) is used. E.g. leukocyte interferon is designated IFN-(alpha)."). This specification language concerning the new nomenclature was added to the specification on February 24, 1983, three years after the initial patent application was filed. The prosecution history cites to a co-pending, continuation-in-part S.N. 223,108 application filed in April of 1980, in which the change was also made to support this specification amendment. *See* D.I. 172, Tab 18 at 9. This cite to the then co-pending application, however, is unhelpful and misleading as this co-pending application was filed: 1) later then the '901 Patent application and 2) after additional interferon genes had been identified. The Court is thus left with the question of whether it is proper to consider this subsequently added specification language in interpreting this claim language.

Schering responds with at least five separate arguments. First, Schering asserts the change from leukocyte interferon to IFN-(alpha) was a simple change in nomenclature and therefore, does not constitute new matter in violation of the patent statute. *See* 35 U.S.C. s. 132 ("No amendment shall introduce new matter into the disclosure of the invention."); *see also* 37 C.F.R. s. 1.118(a) ("No amendment shall introduce new matter into the disclosure of an application after the filing date of the application ...."). Amgen, unsurprisingly, disagrees.

[35] [36] [37] The new matter prohibition under s. 132 is to be interpreted in the same manner as the

identical new matter prohibition found in the reissue statute, 35 U.S.C. s. 251. *See* Application of Oda, 58 C.C.P.A. 1353, 443 F.2d 1200, 1203 n. 2 (CCPA 1971). Because whether the statutory requirements of 35 U.S.C. s. 251 have been met is a question of law, *see* Hester Industries, Inc. v. Stein, Inc., 142 F.3d 1472, 1479 (Fed.Cir.1998) (citing In re Clement, 131 F.3d 1464, 1468 (Fed.Cir.1997)), whether the new matter prohibition under s. 132 is violated must also be a question of law. Nevertheless, the legal conclusion is based on underlying findings of fact, which will be sustained unless they are clearly erroneous. *See* Clement, 131 F.3d at 1468; In re Kemps, 97 F.3d 1427, 1430 (Fed.Cir.1996) ("The law of this circuit is clear: PTO factual determinations are reviewed under the 'clearly erroneous' standard."). Additionally, the presumption of administrative correctness as applied to a new matter determination is "entitled to an especially weighty presumption of correctness." *See* Brooktree Corp. v. Advanced Micro Devices, Inc., 977 F.2d 1555, 1574-75 (Fed.Cir.1992) (quoting In re Smythe, 480 F.2d 1376, 1385 n. 5 (CCPA 1973)).

Despite this heavy burden, the Court is persuaded that the patent examiner's allowance of this "new matter" was clearly erroneous and was incorrect as a matter of law. The patent examiner improperly relied on a subsequently filed, continuation-in-part application by Biogen to allow this amendment to the '901 patent application. However, that continuation-in-part application was filed in April of 1980, both after the '901 Patent application was filed, and more importantly, before even the terminology "IFN-(alpha)" was adopted. This fact is important because as Amgen correctly observes, the change from leukocyte interferon to IFN-(alpha) reflects more than a mere name change, it also represents a substantive modification in the way interferons are to be classified. Relying on extrinsic evidence, as the Court must to aid its interpretation in this area because the intrinsic evidence of the record is muddled, the Nature article states:

Interferons will be classified into types on the basis of antigenic specificities, type designations to be alpha, beta, and gamma, corresponding to previous designations of leukocyte (Le), fibroblast (F) and type II (immune) interferons, respectively. The old terminology of 'leukocyte', 'fibroblast', and 'immune' interferons were, by committee consensus, abolished, as they clearly were misnomers: both leukocytes and fibroblasts can produce each of these two types of interferon ....

Interferon Nomenclature, Nature, vol. 286, p.110 (July 10, 1980). Before the new nomenclature, interferon classifications were cell-specific, i.e., leukocyte, fibroblast or immune; under the new nomenclature, non-cell specific definitions have been adopted, i.e., (alpha), (beta), and (gamma). Although leukocyte cells produces primarily what is now called alpha interferon, they also produce small amounts of the other types of interferon, including fibroblast interferon or beta interferon. Similarly, fibroblast cells produce primarily beta interferon, but also produce small amounts of alpha interferon. Thus, the substitution of "IFN-(alpha)" for "leukocyte interferon" was not a simple nomenclature change, but a change in scientific terminology that reflects an underlying scientific change in the concepts surrounding interferon proteins. Accordingly, the Court finds as a matter of law that the language and citation referring to the Nature article to be new matter under 35 U.S.C. s. 132. *See* Manuel of Patent Examining Procedure, s. 608.04(a) at M-326 (1997) ("Matter not in the original specification ... is usually new matter."). The Court cannot therefore consider this specification language as rightfully part of the specification in its construction of this claim language. *See* Kolmes v. World Fibers Corp., 107 F.3d 1534, 1539 (Fed.Cir.1997); In re Rasmussen, 650 F.2d 1212, 1214 (CCPA 1981); In re Bloch, 20 C.C.P.A. 1180, 65 F.2d 268, 269 (CCPA 1933).

Second, Schering submits that even if the Court is unwilling to consider this subsequently added specification language, this is not a significant fact as the Federal Circuit has in the past construed claim terms not found in the specification by relying on the prosecution history. *See* Ethicon v. United States Surgical, 93 F.3d 1572, 1581 (Fed.Cir.1996). *Ethicon,* however, did not concern a claim term that did not

exist in the art until after the patent application was filed. This difference is significant because claim language must be construed from the point of view of one of skill in the art *at the time the patent application was filed*. *See* Wiener, 102 F.3d at 539 (emphasis added). When this patent application was filed, however, this nomenclature, which designates leukocyte interferon as IFN-(alpha), had not yet been developed and IFN-(alpha) type was unknown in the art.

Third, Schering contends the prosecution history supports its construction of "IFN-(alpha) type." Although the prosecution history is filled with references to "IFN-(alpha) type," *see, e.g.,* D.I. 172, Tab 30 at 8 ("Not a single one of the IFN-(alpha) type genes is isolated to date (between 12 and 15 genes) has an 80-nucleotide HaeIII fragment, as recited by Colby."), all such references were made after the patent application had been filed. Schering asserts prosecution history statements are always made after a patent application has been filed and yet are routinely relied on to discern the meaning of claim language. Nonetheless, in those cases where prosecution history has been utilized, the claim language was not unknown in the art at the time the patent was filed. Further, the Court is disinclined, given principles of claim construction, to add, limit, or vary the scope of the claims based on *post facto* explanations found only in the prosecution history. *See* Markman, 52 F.3d at 980 (proper role of prosecution history is to inform scope and meaning of claim and specification, not to add, vary, or enlarge claim language).

[38] Fourth, Schering argues that since leukocyte interferon was defined by its activity in the disclosure, any protein found to have the same activity must also be covered by the '901 Patent, including the various sub-species of interferon. This simply cannot be. As an initial matter, even Schering agrees that the patent does not cover the interferon proteins encoded by the isolated DNA sequences because such proteins are unpatentable as products of nature. *See* 35 U.S.C. s. 101; Diamond v. Chakrabarty, 447 U.S. 303, 309, 100 S.Ct. 2204, 65 L.Ed.2d 144 (1980). The '901 Patent covers only isolated DNA sequences and recombinant DNA methods for producing the interferon protein. Moreover, patents cannot cover physical phenomena occurring in nature, such as the biological or immunological effect of interferon on viruses. *See* Chakrabarty, 447 U.S. at 309, 100 S.Ct. 2204. Lastly, even if the Court were to find that leukocyte interferon should be defined as it is in the patent by its activity, the Court has previously determined that it would not take into account the IFN-(alpha) nomenclature change in the specification as it is new matter in violation of 35 U.S.C. s. 132. For these reasons, then, the Court declines to define IFN-(alpha) by its activity. FN25

FN25. This conclusion is consistent with the Patent Examiner's finding that the use of the terms "similar immunological and biological activity" in the initial claims to define the polypeptide in question was unduly broad, vague and indefinite because such a phrase is subject to multiple and subjective interpretations. *See* D.I. 172, Tab 17 at 4.

[39] Fifth, Schering argues that having identified one member of a gene family, it is entitled to claim the whole gene family. Schering cites Oka v. Youssefyeh, 849 F.2d 581 (Fed.Cir.1988) for this proposition. *Oka* does indeed stand for the proposition that, "conception of a species within a genus *may* constitute conception of the genus." FN26 *See id*. at 584 (emphasis added). The Federal Circuit went on to say, however, that where there is no evidence that the patented method could be used to derive the other species within the genus, there is no basis for the view that a description or method of making one is applicable to the other. *See id*. In the case at bar, there was similarly no evidence, *at the time of the invention,* that the recombinant DNA method of procuring IFN-(alpha)-1 could be used to derive the other species in the genus. In fact, at the time of the '901 invention, both Dr. Weissmann and Schering have conceded that it was

unknown in the art that there was more than one species of interferon. Thus, even though Dr. Weissmann had in fact derived, using a hybridization probe, the IFN-(alpha)-2 species among 185 positive colonies of transformed bacteria, he did not describe or isolate the separate species in the disclosure to the '901 Patent.FN27 As such, there is no basis for the view that a description or method of making IFN-(alpha)-1 is applicable to the other species of interferon, including IFN-(alpha)-2. Thus, conception of the IFN-(alpha)-1 species within the IFN-(alpha) genus does not constitute conception of the entire IFN-(alpha) genus.

FN26. "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 therefore to be applied in practice." *See* Kridl v. McCormick, 105 F.3d 1446, 1449-50 (Fed.Cir.1997) (citing Coleman v. Dines, 754 F.2d 353, 359 (Fed.Cir.1985) (quoting Gunter v. Stream, 573 F.2d 77, 80 (CCPA 1978) (emphasis omitted)). Conception must include every feature or limitation of the claimed invention. *See* Kridl, 105 F.3d at 1450 (citing Davis v. Reddy, 620 F.2d 885, 889 (CCPA 1980)).

FN27. Indeed, in the specification, Dr. Weissmann went on to identify 95 of the 185 as being most promising as they gave off the strongest hybridization signal. Significantly, what was later found to be IFN-(alpha) > >>-2 was not among this further study group of 95 and y only that group of 95 was tested by Dr. Weissmann for interferon. *See* Col. 27, lines 63-66. In addition, IFN-(alpha)-2 was found in the SN-206 clone; however, this number appears nowhere in the '901 Patent.

[40] Nevertheless, the Court is also unwilling to agree with Amgen that this language should be held invalid for lack of enablement in the specification or for indefiniteness, as claim construction does not concern itself with arguments of invalidity. *See supra* note 13. "[A] district court must exercise its power and duty to say what the claims mean." *See* Digital Biometrics, 149 F.3d 1335, 1344. Because after consideration of the intrinsic evidence the exact meaning of the claim terms remains a mystery, "consideration of extrinsic evidence[is] necessary to determine the proper construction." *See* id. at 1343. Having decided that extrinsic evidence is necessary to construe a claim term, another claim construction principle comes into play. *See id*. Because a patent applicant has the burden to "particularly point [ ] out and distinctly claim [ ] the subject matter which the applicant regards as his invention," 35 U.S.C. s. 112, para. 2, "if the claim is susceptible to a broader and narrower meaning, and the narrow one is clearly supported by the intrinsic evidence while the broader one raises questions of enablement under s. 112, para. 1, [a court should] adopt the narrower of the two." *See* Digital Biometrics, 149 F.3d at 1343 (citing Athletic Alternatives, Inc. v. Prince Mfg., Inc., 73 F.3d 1573, 1581 (Fed.Cir.1996); Ethicon, 93 F.3d at 1581).

Technical publications in the art make clear that "IFN-(alpha)" does indeed refer to what was previously termed "leukocyte interferon." FN28 *See* Nature at 110. Despite that fact, the Court is unwilling to conclude that "IFN-(alpha)" necessarily includes all IFN-(alpha) subspecies. Even though the '901 Patent specification refers to both F IF [fibroblast interferon] and Le IF [leukocyte interferon], the patent specification did not differentiate between different subtypes of leukocyte interferon. *See* Col. 1, lines 36-43. Nor does the fact that the specification refers to the "polymorphic" nature of leukocyte interferon lead the Court to another conclusion. *See* Col. 2, lines 34-35. "Polymorphic" only means that the same polypeptide may manifest itself in slightly different structural variations, not that there are separate subspecies. In addition, in both Weissmann's deposition testimony and in Schering's Opening Brief on Claim Construction, it is candidly admitted that at the time of Dr. Weissmann's invention, Dr. Weissmann did not recognize the existence of multiple alpha interferon subtypes. *See* D.I. 163 at 27; D.I. 176, Ex. L at 319. There is therefore no evidence

in the intrinsic or extrinsic record that the inventor, Dr. Weissmann, knew at the time of the invention that there were various subspecies of interferon protein.

FN28. Such a finding is not to be confused with the fact that such a change in designation was not a mere nomenclature change. Although IFN-(alpha) does correspond to leukocyte interferon in this instance, the fact of the matter remains that leukocyte interferon was a cell-specific definition, while the alpha designation takes into account the fact that such alpha interferons may also produce other types of interferon found in different cells. *See* Nature at 110.

Schering responds in its Opening Brief, however, that, "[a]lthough the Weissmann Inserts apparently all code for a single alpha interferon subtype (which became known as IFN-alpha-1), one skilled in the art could have isolated the DNA coding for the other naturally occurring alpha interferon subtypes ... following the hybridization procedures described in the patent specification." *See* D.I. 163 at 8. In fact, during oral argument, Schering made the observation that the hybridizations disclosed in the specification led to the discovery of 185 positive colonies, one of which later turned out to be the DNA sequence for IFN-(alpha)-2. *See* Col. 27, lines 61-66. Through this logic, Schering attempts to convince the Court to adopt a broader meaning for the term "IFN-(alpha)" by including sub-species not specifically disclosed in the specification, but enabled in the specification.

The Court is not persuaded. There remains a significant question as to whether the specification does disclose and enable the production of the other interferon sub-species. Specifically, although another sub-species was eventually found to exist as part of the hybridization probe carried out in the disclosure, that sub-species was not identified or isolated in the disclosure of the '901 Patent.FN29 Accordingly, because this claim language is susceptible to a broader and narrowermeaning, and only the narrow one is clearly supported by the intrinsic evidence while the broader one raises questions of enablement under s. 112, para. 1, the narrower of the two meanings must be adopted under applicable claim construction principles. *See* Digital Biometrics, 149 F.3d at 1343. Consequently, the Court construes the "IFN-(alpha)" portion of the claim term "IFN-(alpha) type" to refer to a single, naturally-occurring leukocyte interferon protein known at the time of the '901 invention, now referred to as IFN-(alpha)-1.

FN29. In fact, it was not until shortly after the application was filed when Dr. Weissmann was engaged in a conversation with another scientist that the possibility of other subspecies of interferon existing became clear. *See* D.I. 176, Ex. K at 119. Subsequently, Dr. Weissmann isolated and identified the IFN-(alpha)-2 subspecies and filed a continuation-in-part application to cover this invention as well. The question arises, therefore, why would Schering have submitted a continuation-in-part application on this invention if it believed that the invention had already been claimed in its initially filed patent application.

b. Whether "IFN-(alpha) Type" May Refer To Mature Proteins

[41] A closely related question to whether IFN-(alpha) corresponds to more than one protein is whether the claim term "IFN-(alpha) type" covers: 1) DNA sequences coding for the mature form of the interferon protein, i.e., interferon itself; 2) the immature form, i.e., interferon with a leader sequence attached, FN30; 3) a fusion protein, i.e., interferon with additional adjacent amino acids from another gene or tails attached; 4) some combination of the first three; or 5) even a protein with less than the full alpha interferon sequence.FN31 Schering asserts that since "IFN-(alpha)" refers to a mature leukocyte interferon protein, it

follows that "IFN-(alpha) type" may refer to either an immature protein, a fused protein or a mature protein. Amgen disagrees and maintains the '901 Patent covers only immature proteins and fused proteins, but not mature proteins. Because the parties agree that "IFN-(alpha) type" covers immature proteins and fused proteins, the Court will focus its analysis on whether "IFN-(alpha) type" may refer to mature proteins as well.

FN30. The leader sequence facilitates, through a complex biological process, the movement of the translated interferon protein from the cytoplasm of the cell to the outer membrane of the cell. Having performed this function, the leader sequence is cleaved from the protein strand. The interferon protein secreted into the blood stream from the cell, therefore, no longer has a leader sequence attached.

FN31. Schering also argues that the use of "type" in the claim term "IFN-(alpha) type" connotes coverage of all the sub-species of interferon. Having found that "IFN-(alpha)" in the '901 Patent only corresponds to IFN-(alpha)-1, it follows for the same reasons analyzed above that "IFN-(alpha) type," as used in the '901 Patent, also only covers IFN-(alpha)-1. There is thus no need at this point to consider this separate argument advanced by Schering.

The '901 Patent is silent as to the import of the word "type" in the claim language. Nevertheless, "IFN-(alpha)" by itself, without the word "type" appended, appears nowhere in the claim language. If Schering had wanted its patent to read on both "IFN-(alpha)" and "IFN-(alpha) type" polypeptides, it could have written the claim language to reflect that both forms of the polypeptide were covered. It is therefore irrelevant that "IFN-(alpha)" may indeed correspond to a mature IFN-(alpha)-1 protein.

[42] Supporting this reading of the claim language is the fact that polypeptides of the "IFN-(alpha) type" are all that is supported by the intrinsic evidence of the patent. For instance, the specification recites:

[A]ntibodies directed against human Le IF [leukocyte interferon] specifically inhibit the IF [interferon] of polypeptides produced in E. coli transformed with certain recombinant DNA molecules containing the HcIF-2h DNA sequences. The apparent lower affinity for the IF produced in E. coli may reflect structural differences between the latter and natural Le IF, for example, absence of carbohydrate moiety, presence of signal sequence, or fusion to part of the (beta)-lactamase sequence.

Col. 34, lines 50-58; *see also* Col. 30, lines 26-32. This passage reflects that the inventor was aware that he had not isolated the interferon gene alone, but had produced variations with structural differences, including interferon with a signal sequence (immature proteins), with parts of another gene (fused proteins), or a protein with less than the full alpha interferon sequence.FN32 Additionally, the specification points out that Dr. Weissmann had to fuse nucleotide "tails" to the DNA in order to insert the DNA sequences into the plasmid cloning vector. *See* Col. 14, lines 12-48. In fact, Schering admits that the DNA inserts deposited at the DSM are DNA sequences coding on expression for immature or fused forms of IFN-(alpha)-1. *See* D.I. 163 at 8, 30. Nevertheless, Schering cites to the following language in the specification for the proposition that the '901 Patent teaches how to produce a mature protein:

FN32. Amgen argues that "a polypeptide of the IFN-(alpha) type" must also cover DSM 1699, a DNA insert mentioned in claims 5 and 8, which corresponds to DNA fragment 4C. *See* Col. 36, line 48-49; Col. 37, line5-6. DNA fragment 4C, however, only codes for a part of the mature alpha interferon gene. Schering

retorts that paragraph (b) and (c) of Claim 1, *see infra* note 17, do not cover DSM 1699 because it is too short to "code on expression for a polypeptide of the IFN-(alpha) type."

The Court is persuaded, however, that DSM 1699 is covered by both paragraphs (b) and (c) because the claim language refers to DNA which hybridize to any of the foregoing DNA inserts and which code on expression for a polypeptide of the IFN-(alpha) type. *See* Col. 36, lines 53-59; Col. 37, lines 10-17. Significantly, the hybridizing DNA need not code on expression for IFN-(alpha), but only for an IFN-(alpha) type, which could conceivably cover incomplete alpha interferon amino acid sequences. The Court therefore also finds that "a polypeptide of the IFN-(alpha) type" may include DNA sequences which code on expression for less than the full alpha interferon amino acid sequence.

It is thus of advantage to separate the specific coding sequences for the desired protein from their adjacent nucleotide sequences and fuse them instead to other known expression control sequences so as to favor higher levels of expression .... Therefore, to improve the production of a particular polypeptide in an appropriate host, the gene coding for that polypeptide may be prepared as before and removed from a recombinant DNA molecule containing it and reinserted into a recombinant DNA molecule closer to its former expression control sequence or under control of one of the above expression control sequences. Such methods are known in the art.

Col. 32, lines 30-35; 53-59. Although this language deals with eliminating fusion proteins, this segment of the specification does not deal with the elimination of the leader sequence. Notably absent from this description is any mention of the leader sequence or any mention of the distinction between immature and mature proteins. Stating it is "of advantage" to separate the specific coding sequence for the desired protein is not tantamount to saying that the leader sequence is also eliminated, especially since the subsequent method outlined in the specification does not say the leader sequence will be thereby eliminated or that even all of the fused proteins will be eliminated. As a consequence, the patent does not teach how to produce the interferon protein alone without additional, adjacent amino acids attached.

In any event, a crucial distinction must be made in claim construction between importing an additional limitation into the claim, which is improper, and looking to the specification to aids its interpretation of a term already in the claim, an entirely appropriate practice. *See* Ethicon, 93 F.3d at 1578. In this instance, even assuming for the sake of argument that "IFN-(alpha)" does refer to the mature form of leukocyte interferon, the fact of the matter is that "IFN-(alpha)" does not appear in the *claim*. Only "IFN-(alpha) type" does. Thus, by reading "IFN-(alpha)type" to refer to the mature form of the protein, the Court in effect would be improperly importing the term "IFN-(alpha)" into the claim. This type of m claim construction is improper and impermissible.

Further, although there are numerous passages from the prosecution history which utilize the term "IFN-(alpha) type," *see, e.g.,* D.I. 172, Tab 18, at 14-15, there is no intrinsic evidence that this term was understood in the manner utilized in the prosecution history at the time the '901 patent application was filed, i.e., January of 1980. Without some basis in fact that "IFN-(alpha) type" had the same meaning when the patent application was filed, the Court is unwilling to vary the scope of this claim language based on the prosecution history alone. *See* Markman, 52 F.3d at 980. In short, the Court is unable to find intrinsic evidence that Dr. Weissmann had the ability to produce the mature form of the interferon protein without a leader sequence at the time the patent application was filed.

Because "type" of "IFN-(alpha) type" is not defined in any unusual manner in the specification or the prosecution history, the Court is constrained to apply its ordinary and customary meaning. *See* Vitronics, 90 F.3d at 1582. "Type" is defined in the dictionary as meaning "something that serves as a symbolic representation usu. of a thing yet to come into being; something felt to be distinguishable as a variety or

kind." *See* Webster's at 2476. This dictionary definition lends added support to the conclusion that the IFN-(alpha) type polypeptide does not include the final or complete form of the interferon protein, i.e., without the leader sequence attached or with less than the full alpha interferon. Instead, these interferon proteins serve as a representation of, and share many common features with, the mature form of interferon. The use of the word "type," however, signifies to the reader of the patent that only varieties of the "IFN-(alpha)" protein were known, distinguishable from the mature interferon protein, which at that time had not yet come into being.

Based on this analysis, the Court concludes that the addition of the term "type" to the "IFN-(alpha)" refers to the fact that the interferon protein could only be produced in its immature, fused and/or incomplete forms. Accordingly, the claim language "IFN-(alpha) type" refers to an immature, fused and/or incomplete form of a human leukocyte interferons, subsequently labeled IFN-(alpha)-1, but not, as Schering suggests, to the mature form of IFN-(alpha)-1.

Combining the two portions of the "polypeptides of the IFN-(alpha) type" claim construction, the Court holds that "a polypeptide of the IFN-(alpha) type" refers to a immature, fused, and/or incomplete form of a naturally occurring, human leukocyte interferon protein, subsequently labeled "IFN-(alpha)-1." It is emphasized the Court finds that this claim language does not cover mature leukocyte interferon or other, later-discovered sub-types of leukocyte interferon such as IFN-(alpha)-2.

6. "(b) DNA sequences ... which code on expression for a polypeptide of the IFN-(alpha) type, and (c) DNA sequences which code on expression for a polypeptide of the IFN-(alpha) type coded for on expression by any of the foregoing DNA sequences and inserts ...."

[43] The crux of the dispute between the parties with regard to this claim language is the meaning of the claim terms "DNA sequences" and "code on expression." Schering argues that subparagraph (c) should be interpreted to add interchangeable DNA sequences which also code for polypeptides that are coded for by the deposited DNA inserts or the related hybridizing DNA sequences.FN33 Further, Schering contends this claim language is not limited to only naturally occurring, interchangeable DNA sequences. Amgen, on the other hand, would require that the DNA sequences not only code for the desired polypeptide, but that the encoded polypeptide is actually produced by being transcribed and translated into the corresponding protein. Moreover, Amgen asserts all the DNA sequences must be naturally occurring as the claim language "segments of DNA from different genomes" applies to all the subparagraphs, including (b) and (c).

FN33. Because multiple codons may code for the same amino acid, alternative nucleotide sequences may code for the same proteins. This redundancy of the genetic code is referred to as its degenerative nature.

First, the Court finds that the claim language "segments of DNA from different genomes," *see* Col. 36, line 4-5, applies to the DNA sequences described in subparagraphs (b) and (c). By the terms of the claim itself, these "segments of DNA" "consist of" those DNA sequences described in subparagraph (b) and (c). *See* Col. 36, lines 4-20. Consequently, the construction of "segments of DNA from different genomes" must also apply to the "DNA sequences" of subparagraphs (b) and (c). As the Court has held that "segments of DNA from different genomes" refers to both naturally occurring and non-naturally occurring DNA segments or sequences, the "DNA sequences" of subparagraph (b) and (c) are similarly not limited to naturally-occurring DNA sequences.

As for the meaning of "code on expression," the Court starts its analysis with the relevant claim language. Subparagraph (c) requires the DNA sequences described therein to have two attributes. First, the DNA sequences must code on expression for a polypeptide of the IFN-(alpha) type. *See* Col. 36, lines 17-18. In other words, the DNA sequences must code on expression for an immature, fused, and/or incomplete, naturally occurring, human leukocyte interferon protein, subsequently labeled "IFN-(alpha)-1." Second, the polypeptide of the IFN-(alpha) type has to also be coded on expression by any of the foregoing DNA inserts and sequences set forth in either subparagraph (a) or (b), i.e., the DNA inserts deposited at the DSM or DNA sequences which hybridize to the DNA inserts. *See* Col. 36, lines 10-20.

Thus, subparagraph (c) does not cover any new interferon proteins; it must code on expression for a polypeptide of the IFN-(alpha) type. However, if there is a DNA sequence equivalent on expression to either the DNA inserts of subparagraph (a) or DNA sequences which hybridize thereto under subparagraph (b), those DNA sequences are covered by subparagraph (c). This conclusion only makes sense because of the degenerate nature of the genetic code; that is, different codons (nucleotide triplets) can code on expression for the same amino acids. For instance, if a DNA insert had the following nucleotide sequence: AGGTCGGCA, it would code on expression for the following amino acids: Arginine-Serine-Alanine. However, the following degenerate nucleotide sequence would also code on expression for the same chain of amino acids: CGCTCCGCC, and therefore would also produce the same polypeptide. Subparagraph (c) therefore covers degenerate sequences to the DNA inserts, or DNA sequences which hybridize thereto, and which also code on expression for a polypeptide of the IFN-(alpha) type. *See* Col. 28, lines 8-14 ("It is also to be understood that DNA sequences, which are not screened by the above DNA sequences, yet which as a result of their arrangement of nucleotides code on expression for the polypeptides coded for by the expression of the above DNA sequences also fall within this invention.").

Having analyzed the claim language, the Court finds that these DNA sequences must only code on expression for the desired polypeptide, but need not actually produce the polypeptide by transcription and translation and subsequently, be detected. The knowledge that a given DNA sequence will produce on expression a given polypeptide is sufficient. There is no basis for the belief that the identified and isolated DNA sequences must be transcribed, translated and then detected. The claim language is clear that it is the DNA sequences that are covered by the claim, not the proteins that are eventually coded for on expression.

The specification is in accord. Although the specification specifically sets out a definition for "expression," *see* Col. 7, lines 3-5, the claim language does not read "DNA sequences expressing a polypeptide of the IFN-(alpha) type," but "DNA sequences which code on expression for a polypeptide of the IFN-(alpha) type." The latter phrase points to the fact that *if* the DNA sequences were decoded, a polypeptide of the IFN-(alpha) type would be produced. However, only the former language, not in the '901 Patent, requires actual expression of the desired polypeptide.

This interpretation is also supported by the prosecution history of the '901 Patent. Initially, subparagraph (b) was amended to recite "code for a polypeptide of the IFN-(alpha) type." *See* D.I. 172, Tab 18 at 3. Subparagraph (c), on the other hand, was initially amended to state: "DNA sequences which code for a polypeptide coded for by any of the foregoing DNA sequences." *See* id. Amgen contends that the phrase "code for" initially utilized by Schering would have allowed for just the recitation of the DNA sequence; however, "code on expression" points to the fact that the patent examiner was concerned that the DNA sequences may not properly express the polypeptide. Accordingly, Amgen argues the polypeptide must be transcribed from the corresponding DNA template, translated from the RNA, and subsequently detected.

A closer reading of the relevant prosecution history shows that Amgen is mistaken in its analysis. Specifically, the patent examiner found the "code for" phrase to be vague "because it is not clear whether applicant intends to claim all of the possible coding sequences that may result from (a) frame-shifts and/or (b) silent mutations." *See* D.I. 172, Tab 21 at 4. That is, the patent examiner was unclear whether Biogen wanted to claim all DNA sequences which code for a polypeptide of the IFN-(alpha) type, but subsequently through frame shifts or mutations produced a variant coding sequence. Biogen amended "code for" to "code on expression" to make clear that is was only concerned with the DNA sequences which actually were able to code on expression for the desired polypeptide. However, there is no basis in fact for Amgen's conclusion that the patent examiner was requiring that proteins actually be produced and detected. Thus, the prosecution history does not support Amgen's interpretation of this claim language.FN34

FN34. Even if the Court were to agree with Amgen's reading of the prosecution history, the claim language clearly covers only the DNA sequences. *See* Col. 36, lines 14-20. Because the claim language, which is the best guide to the meaning and scope of a patent, trumps the prosecution history, *see* Phonometrics, 133 F.3d at 1464, the Court's conclusion would not be altered.

The Court holds that "(b) DNA sequences ... which code on expression for a polypeptide of the IFN-(alpha) type, and (c) DNA sequences which code on expression for a polypeptide of the IFN-(alpha) type coded for on expression by any of the foregoing DNA sequences and inserts" refer to both naturally occurring and non-naturally occurring DNA sequences which bear the genetic code for expressing the polypeptide; actual expression and detection of the protein, however, is not required.

B. Claim 8

1. "Substantially pure DNA sequence ... coding on expression for only a single polypeptide chain"

[44] The Claim 8 FN35 dispute revolves around the meaning of "substantially pure." Schering contends that a mathematical degree of purity is not required, but only that the desired DNA segment must be identified and available for purposes of conducting a hybridization probe for identifying related DNA sequences and for using in a plasmid to express the alpha interferon in the host cell. Additionally, Schering maintains a DNA sequence remains substantially pure even if it is synthetically derived and subsequently, inserted into a particular cloning vehicle (plasmid) and used to express a protein. Amgen counters this contention by arguing that a DNA sequence is "substantially pure" when naturally-occurring DNA is isolated from other DNA sequences. Accordingly, Amgen disagrees with Schering that a DNA sequence may be synthetically derived and that it may be simultaneously "substantially pure" and part of a plasmid within a host cell.

FN35. Claim 8 reads:
8. A substantially pure DNA sequence selected from the group consisting of: (a) the DNA inserts of Z-pBR322(Pst)/HcIF-4c (DSM1699), Z-pBR322(Pst)/ HcIF-2h (DSM 1700), Z-pBR322(Pst)/HcIF-SN35 (DSM 1701), Z-pBR322(Pst)/HcIF-SN42 (DSM 1702) and Z-pKT287(Pst)/HcIF-2h-AH6 (DSM 1703), (b) DNA sequences which hybridize to any of the foregoing DNA inserts and which code on expression for a polypeptide of the IFN-(alpha) type, and (c) DNA sequences which code on expression for a polypeptide of the IFN-(alpha) type coded for on expression by any of the foregoing DNA sequences and inserts, said DNA sequences coding on expression for only a single polypeptide chain.
Col. 37, lines 3-17.

Consulting the language of the claim first as required under applicable claim construction principles, *see* Phonometrics, 133 F.3d at 1464, "substantially pure DNA sequences" are selected from a group consisting of: the previously discussed DNA inserts (Group A), DNA sequences which hybridize to the DNA inserts and which code on expression for a polypeptide of the IFN-(alpha) type (Group B), and DNA sequences which code on expression for polypeptide of the IFN-(alpha) type coded for on expression by any of the foregoing DNA sequences and inserts and coding on expression for only a single polypeptide chain (Group C). *See* Col. 37, lines 3-17. As for the Group A DNA sequences, although these DNA inserts have been deposited in the DSM as part of engineered plasmids in bacterial host cells that produce the desired interferon protein, the language of the claim specifically recites that it is the "DNA inserts," not the surrounding plasmid or host cell, that make up the "substantially pure DNA sequences." *See* Col. 37, lines 3-9. Similarly, only the "DNA sequences" of Group B and C are covered by the claim language. *See* Col. 37, lines 10-17. It follows the claim language itself makes clear that "substantially pure DNA sequences" refer to DNA sequences separate from the plasmid or bacterial host cell into which they are incorporated.

This interpretation of "substantially pure DNA sequences" is consistent with other claim terms already construed. *See* Southwall, 54 F.3d at 1579 (claims in the same patent are to be interpreted with reference to one another). Just as the construction given to "a polypeptide of the IFN-(alpha) type" only includes the immature, fused, and/or incomplete forms of leukocyte IFN-(alpha)-1, the DNA sequences are only "substantially pure" because they also may include additional adjacent nucleotides or have less than the full mature IFN-(alpha)-1 nucleotide sequence. In other words, the phrase "substantially pure" has nothing to do with a specific degree of purity, but only reflects that fact that the DNA sequences which code of expression for IFN-(alpha)-1 may be surrounded by additional adjacent nucleotides or be incomplete. Additionally, Claim 8 requires that the "[s]ubstantially pure DNA sequence ... cod[e] on expression for only a single polypeptide chain." *See* Col. 37, lines 3, 16-17. If, however, this DNA sequence were to be bound up with plasmid DNA of the bacteria host, more than a single polypeptide chain would be produced in violation of the explicit claim limitation. Further, this interpretation is in conformity with the structure of the '901 Patent as a whole. *See* Southwall, 54 F.3d at 1579 (individual patent claims should be construed in reference to one another). It is only in the other claims of the '901 Patent that the substantially pure DNA sequences are ligated to the foreign plasmid DNA, through the use of the Pst I restriction enzyme, to form the desired recombinant DNA molecule, *see* Col. 36, lines 4-24 (Claim 1), and subsequently transform a unicellular host. *See* Col. 36, lines 40-59 (Claim 5).

Nor does the specification support Schering's construction of this claim language. Although Schering admits that "substantially pure" is not used in the specification, it nevertheless points to an unrelated phrase, "sufficiently purified sample of IFmRNA or DNA ... to act as a screening probe for the identification of the desired clones," *See* Col. 9, lines 66-69, as evidence that the substantially pure DNA sequences may be part of a plasmid in a host cell. This language, however, refers to the use of purified IFmRNA or cDNA as a hybridization probe, not to DNA sequences which express interferon in its active form. *See* Col. 10, lines 7-14. Additionally, this specification language makes no reference to plasmid DNA and/or host cell DNA. In any event, to use the cDNA and IFmRNA as screening probes, one of the explicit functions set out for these DNA sequences by Schering itself, they necessarily have to be separated from other plasmid and host cell DNA. All the other uses of the word "purified" in the specification are similarly unrelated to the disputed claim language in Claim 8. *See* Col. 24, line 66 through Col. 25, lines 14.

The prosecution history is more ambiguous in this regard. Schering cites the prosecution history for the proposition that substantially pure DNA sequences may be part of a plasmid in a host cell. In substituting

the phrase "substantially pure DNA sequence" for "gene" in response to the examiner's rejection that "gene" refers to a product of nature in violation of 35 U.S.C. s. 101, Schering asserts that it made clear that the DNA sequences were substantially pure in this invention because

Before this invention such sequences may have been located somewhere among about the five billion nucleotides of the human chromosome. There, they were plainly not available for use in the production of interferon as described in this application. There, they were plainly not 'substantially pure.' Accordingly, the claimed sequences do not occur 'substantially unaltered' in nature. They are therefore patentable under 35 U.S.C. s. 101.

See D.I. 172, Tab 11 at 8. Schering therefore used the phrase "substantially pure" to convey the idea that the interferon gene in question had been isolated, prepared and used for the first time in this invention. Schering urges these DNA sequences are pure in the sense they are separated from the nearly five billion nucleotides of the human chromosome. Schering goes on to argue that the DNA sequences are "substantially pure" in that where before they were part of five billion nucleotides, now they are only part of a bacterial plasmid made up of about five thousand nucleotides. So in comparison,the argument goes, these DNA sequences are "substantially pure."

An equally good argument could also be made that the reason these DNA sequences are considered "substantially pure," rather than just "pure," is because the nucleotide sequence that codes on expression for IFN-(alpha)-1 may have attached to it extraneous, additional nucleotides which code on expression for a leader sequence, fusion proteins, or other extraneous amino acids from adjacent genes on the human chromosome or tails used for ligation purposes. This line of reasoning could also lead to the conclusion that the DNA sequences were at one time or another ligated to plasmid DNA and thus, could be "substantially pure" and still part of the bacterial plasmid within a host cell.

In the end, the correct interpretation of the prosecution history cited above is irrelevant to the Court's analysis. Even assuming for the sake of argument that the prosecution history did allow for the DNA sequences which code for IFN-(alpha)-1 to be attached to DNA sequences from adjacent plasmid DNA, such an interpretation would be inconsistent with the claim language which only covers the DNA inserts and DNA sequences and does not cover the plasmid DNA to which it is ligated or the bacterial host which it transforms. Under such circumstances, the claim language which is the best guide to the meaning and scope of a patent must prevail over the prosecution history. *See* Phonometrics, 133 F.3d at 1464 (claim language is foremost in importance); *see also* Markman, 52 F.3d at 980 (prosecution may not enlarge, diminish or vary the limitations in the claim). The Court therefore find that "substantially pure" DNA sequences refer to the DNA sequences alone and apart from plasmid DNA in a bacterial host cell.

At the same time, the Court is persuaded that "substantially pure DNA sequences" can be both naturally occurring and non-naturally occurring DNA sequences. As demonstrated above, substantial purity has nothing to do with a mathematical degree of purity or with natural versus synthetic DNA sequences. The purity in question only refers to the alpha interferon DNA being separated, isolated and identified apart from the human genome and any other relevant bacterial genome.FN36 Further, the specification discloses that nucleotide tails must be added to both the DNA sequences and the spliced plasmid DNA in order to ligate the two components together. If these tails are part of the subsequent substantially pure DNA sequences, there is a segment of the DNA sequences that appears nowhere in nature. *See* Col. 13, lines 6-21. Additionally, the following specification language contemplates DNA sequences which do not occur in nature:

FN36. Schering observes that the DNA inserts deposited at the DSM are actually cDNA, which is DNA synthetically derived in a test tube using enzymes. However, the Court does not believe that this is the distinction Amgen wishes to make. Amgen is not concerned whether copies of naturally-occurring DNA can be used, but whether DNA that occurs nowhere in nature may be used. Schering's argument is therefore unresponsive to Amgen's contention.

It is, of course, evident that this method of clone screening may be employed equally well on other clones containing DNA sequences arising from recombinant DNA technology, synthesis, natural sources or a combination thereof ....
See Col. 27, line 67 through Col. 28, line 3.
The prosecution history also supports this construction. The examiner did in fact reject the following claim language:

DNA sequences from whatever source obtained, including natural, synthetic or semi-synthetic sources related by mutation, including single or multiple, base substitutions, deletions, insertions and inversions to [any of the foregoing DNA sequences].

See D.I. 172, Tab 1 at 68. This language was replaced by "DNA sequences which code for a polypeptide coded for by any of the foregoing DNA sequences." *See* D.I. 172, Tab 18 at 6. However, as explained above, the correction was made not to address the examiner's concerns about synthetic or semi-synthetic DNA sequences, but to address the problem of base substitutions, inversions and mutations which could potentially cover the whole human genome. *See* D.I. 172, Tab 17 at 3-4. Thus, the prosecution history does not now estop Schering from asserting that "substantially pure DNA sequences" include both naturally-occurring and non-naturally occurring sequences.

The Court holds the claim language "substantially pure DNA ... coding on expression for only a single polypeptide chain" refers to a naturally occurring or non-naturally occurring DNA sequence, independent of any plasmid DNA in a host cell, which codes on expression for an immature, fused, and/or incomplete form of a naturally occurring human leukocyte interferon protein, subsequently labeled IFN-(alpha)-1.

An appropriate order will issue.

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