IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

DIGENE CORPORATION,	:	
Plaintiff,	:	
v.	:	C.A. No. 01-752-MPT
VENTANA MEDICAL SYSTEMS, INC. and BECKMAN COULTER, INC.,	:	
Defendants.	:	

MEMORANDUM ORDER

INTRODUCTION[1]

This is a patent infringement case. On November 19, 2001 Digene Corporation ("Digene") filed a complaint against Ventana Medical Systems, Inc. ("Ventana") for willful infringement of United States Patent Nos. 4,849,331 ("the '331 patent") and 4,849,332 ("the '332 patent") (collectively "the patents-in-suit") in conjunction with the development, manufacture, marketing, sales, and offers for sale of its INFORM® HPV High Risk Probe and in its INFORM® HPV Low Risk Probe Products.[2] Digene further alleged that Ventana willfully induced others to infringe the patents-in-suit.[3] In the initial complaint, Digene sought, among other things, damages for Ventana's past

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[1] A detailed recitation of the relationship of the parties and transactions among the parties to this litigation, their predecessors in interest, and other third parties is found in *Digene Corporation v. Ventana Medical Systems, Inc.*, 316 F. Supp. 2d 174 (D. Del. 2004), familiarity with which is assumed by the reader.

[2] D.I. 1, ¶¶ 7,8.

[3] *Id.*, ¶ 9.

infringement, enhanced damages, and attorneys' fees for Ventana's willful infringement, and an injunction against Ventana's continued infringement.[4] On February 2, 2002, Ventana answered the complaint, denying infringement and raising several defenses, including the affirmative defense that its allegedly infringing activities are licensed under the '332 patent.[5]

On September 23, 2002, Ventana and Beckman Coulter, Inc. ("Beckman") executed an Asset Purchase Agreement (the "2002 APA"), which provided that Ventana would purchase Beckman's entire right, title and interest in certain assets, including rights under a 1991 sublicense between Institut Pasteur ("IP") and Beckman.[6] On October 18, 2002, Digene moved for leave to file an Amended Complaint,[7] which the court granted on December 10, 2002.[8] On December 13, 2002, Digene filed its Amended Complaint, adding Beckman as a defendant and additional claims, including civil conspiracy.[9] On December 27, 2002, Ventana filed a motion to compel arbitration, to the stay proceedings, and to dismiss the conspiracy claim in the Amended Complaint.[10]

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[4] *Id.*, ¶ 10.

[5] D.I. 6.

[6] *Digene*, 316 F. Supp. 2d at 182.

[7] D.I. 93.

[8] D.I. 118.

[9] D.I. 119.

[10] D.I. 125. Beckman also filed a motion seeking, among other things, that the court compel Digene to arbitrate its claims against Beckman. *Digene*, 316 F. Supp. 2d at 175; D.I. 128. On March 1, 2004, the court denied several of the parties' motions, without prejudice, including Ventana's motion to dismiss the conspiracy claim of the Amended Complaint. *See* D. I. 260.

On January 28, 2003, Digene moved for leave to file a Second Amended Complaint ("SAC").[11] Leave was granted by the court,[12] and the SAC was deemed filed on March 5, 2003.[13] Count IV of the SAC asserts a claim for civil conspiracy.[14]

On May 7, 2004, the court ordered Digene and Beckman to arbitration and stayed this case pending the outcome of that arbitration.[15] Arbitration took place during March 2006 and the arbitration panel issued its award on July 27, 2006.[16] The court lifted the stay of these proceedings on August 15, 2006.[17] On August 29, 2006, the parties filed several motions. Ventana filed a motion to dismiss the civil conspiracy claim, Count IV, of the SAC.[18] On March 6, 2007 the court granted Ventana's motion to dismiss Count IV of the SAC.[19] Digene filed a motion requesting that the court preliminarily enjoin Ventana from making, using, offering for sale, selling, licensing, or otherwise distributing products which purportedly embody or comprise the inventions

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[11] D.I. 139.

[12] D.I. 160.

[13] D.I. 174.

[14] *Id.*, ¶¶ 65-67.

[15] *Digene*, 316 F. Supp. 2d at 186.

[16] *See* D.I. 332 at 2.

[17] D.I. 297. On January 23, 2007, the parties consented to the jurisdiction of the United States Magistrate Judge, pursuant to 28 U.S.C. § 636(c) and Federal Rule of Civil Procedure 73, to conduct all proceedings and enter the order of judgment and the case was referred to the magistrate judge on the same date. D.I. 400.

[18] D.I. 309.

[19] D.I. 416.

claimed in the '332 patent.[20] The court denied that motion on May 9, 2007.[21] Beckman filed a motion to dismiss Digene's action against it as *res judicata*[22] which the court granted on June 12, 2007.[23]

Trial is scheduled to commence on December 17, 2007. Currently before the court are the parties' proposed claim constructions for disputed claim terms in the '331 and '332 patents.

BACKGROUND OF THE INVENTIONS

The patents-in-suit relate "to nucleic acid hybridization probes for human papillomavirus types and particularly for human papillomavirus type 35 (hereinafter 'HPV 35') [and human papillomavirus type 44 (hereinafter 'HPV 44')]; and methods for employing the same."[24] Human papillomavirus ("HPV") infections are known to cause various lesions, ranging from benign warts to cervical cancer.[25] "HPVs are grouped into types based on the similarity of their DNA sequence."[26] HPV types can be identified via liquid hybridization or epidemiological distribution among genital lesions.[27] Some HPV

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[20] D.I. 314.

[21] D.I. 425.

[22] D.I. 311.

[23] D.I. 447.

[24] '332 patent, 1:7-10. Because the '332 and '331 patents share a substantially similar specification, with examples, figures, and claims which relate to the specific HPV type being the primary difference, the court's citation to particular specification language in either of Digene's patents-in-suit is understood to refer to the same language in each patent, although the corresponding language may not appear in the same column or line in each patent.

[25] '332 patent, 1:14-26.

[26] '332 patent, 1:38-39.

[27] '332 patent, 1:39-2:15.

types are thought to be associated with a greater risk of cervical cancer. Therefore, "the determination of HPV types has clinical-diagnostic value, i.e., such as an important factor in the assessment of risk of cancer development in patients who exhibit evidence of HPV infection. Based on the assessed risk of cancer development, appropriate therapeutic treatments can be selected."[28] The inventions describe "[a] previously unknown HPV type . . . and designated HPV 35."[29]

The parties request that the court construe three claim terms of the patents-in-suit: (1) "HPV 35", (2) "HPV 44", and (3) "fragments thereof."

Claim 1 of the '332 patent is representative of all the asserted claims for the purpose of the disputed terms "HPV 35" DNA and "fragments thereof" and reads: "[a] recombinant DNA of *HPV 35* comprising a cloning vector and substantially all of HPV 35 DNA or *fragments thereof.*"[30]

THE COURT'S CLAIM CONSTRUCTION

At Wilmington, this 24th day of August, 2007, having reviewed the papers submitted with the parties' proposed claim constructions and having considered all of the parties arguments (whether or not explicitly discussed below);

IT IS ORDERED that the disputed claim language in asserted claims of the patents-in-suit, as identified by the parties, shall be construed consistent with the tenets

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[28] '332 patent, 2:32-57.

[29] '332 patent, 6:20-21. The '331 patent describes the identification of a previously unknown HPV type designated HPV 44. '331 patent, 6:21-21.

[30] '332 patent, claim 1, 17:31-33 (emphasis added). Claim 1 of the '331 patent similarly reads: "A recombinant DNA of *HPV 44* comprising a cloning vector and substantially all of HPV 44 DNA or *fragments thereof.*" '331 patent, claim 1, 17:15-17 (emphasis added).

of claim construction set forth by the United States Court of Appeals for the Federal Circuit in *Phillips v. AWH Corp.*,[31] as follows:

1. "HPV 35" ('332 patent)

Digene's proposed construction is:

> (1) an HPV whose DNA hybridizes to greater than 50% to the HPV DNA in clones 2A and 2B under moderately stringent conditions or
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> (2) an HPV whose DNA shows substantially the same epidemiological distribution of cross-hybridization among genital lesions as HPV 35 and that cross-hybridize under stringent conditions with the same genital lesions which comprise the HPV 35 epidemiological distribution.[32]

Ventana's proposed construction is:

> An HPV where its DNA or RNA and ATCC Nos. 40330-40331:
>
> (1) cross-hybridize to greater than 50%, as measured by hybridization in solution under moderately stringent hybridization conditions, or
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> (2) show substantially the same epidemiological distribution of cross-hybridization among genital lesions and cross-hybridize with the same genital lesions which comprise the epidemiological distribution.[33]

The court adopts Ventana's proposed construction.

The parties agree that HPV 35 and HPV 44 should be defined in relation to respective HPV samples deposited with the American Type Culture Collection ("ATCC").[34] The parties also agree that the specification describes two ways to define

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[31] 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*).

[32] D.I. 440, Ex. F.

[33] D.I. 439 at 7.

[34] Ventana's proposed constructions identifies the samples by ATCC number (40330-40331 with respect to HPV 35 and 40353 with respect to HPV 44). Digene's proposed construction identifies the samples by clone number ("2A" and "2B" with respect to HPV 35 and "2" with respect to HPV 44). The specification makes clear that the parties' respective references are the same. *See* '332 patent, 6:37-39 ("HPV 35 clones 2A and 2B have been deposited at the American Type Culture Collection under ATCC

HPV 35 and HPV 44: (1) through liquid hybridization and (2) through epidemiological distribution.

First, the respective HPV types can be identified based on a liquid hybridization test. An HPV which cross-hybridizes with the respective clone (or ATCC deposit) to greater than 50%, as measured by the amount of hybridization in solution under moderately stringent conditions qualifies as HPV 35 (or HPV 44).[35] The parties do not dispute the construction of HPV 35 and HPV 44 with respect to this first test to identify the respective HPV types and the proposed construction of each is substantially identical.

The parties disagree over the construction of the second of the alternative tests, the epidemiological distribution test. The specification states that:

> [W]ithin the context of the present invention, two HPVs are considered to be of the same type if either (1) they meet the criterion for the degree of cross-hybridization discussed above[, greater than 50% hybridization under moderately stringent hybridization conditions,] or (2) *if they show substantially the same epidemiological distribution of cross-hybridization among genital lesions and they both cross-hybridize with the same genital lesions which comprise the epidemiological distribution.*[36]

The difference in the parties' proposed constructions is that Digene's construction requires that cross-hybridization occurs "under stringent conditions" while

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Nos. 40330 and 40331, respectively."); '331 patent, 6:36-38 ("HPV 44 clone 2 has been deposited at the American Type Culture Collection under ATCC No. 40353").

[35] *See* '332 patent, 1:39-48 ("Two HPVs are classified as being of the same type if their DNAs cross-hybridize to greater than 50%, as measured by hybridization in solution under moderately stringent hybridization conditions, which are defined as approximately 25° C. below the melting temperature of a perfectly base-paired double-stranded DNA (conveniently written as t_m – 25° C.), followed by chromatography on hydroxyapatite to separate double-stranded DNA from single-stranded DNA."); '331 patent, 1:39-48 (same).

[36] '332 patent, 2:63-3:2 (emphasis added); '331 patent, 2:63-3:2 (same).

Ventana's construction does not include that requirement.[37] Each party cites the above-quoted section as supporting their position. The court notes, however, that the requirement that cross-hybridization occur under stringent conditions, as proposed by Digene, is not found in that language.[38]

Ventana argues that Digene's proposed construction improperly imports a limitation from a particular embodiment described in the specification. In an example of the epidemiological distribution test, the specification states that:

> In order to demonstrate that hybridization probes prepared from HPV 35 clones 2A and 2B hybridize efficiently under *stringent* conditions only to HPV 35 DNA, and that these hybridization probes can be used to detect genital lesions which contain HPV 35 and to distinguish such genital lesions from genital lesions which contain the DNA of other HPV types, e.g., 6, 11, 16, 18, 31 or 33, the DNA of a collection of cervical biopsies and cervical swabs containing exfoliated cells . . . were analyzed by nucleic acid hybridization under *stringent* and *non-stringent* conditions, for the presence of specific HPV DNAs using probes specific for various HPV types, including probes specific for HPV 35.[39]
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> Thereafter, hybridization was carried out under *stringent conditions* as described above with nick translated ^{32}P-labelled [sic] HPV DNAs from the types discussed above. (For HPV 35 DNA, a mixture of HPV DNA from

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[37] Stringent hybridization conditions "are defined as approximately 10° C. below the melting temperature of a perfectly base-paired double-stranded DNA . . . ." '332 patent, 3:36-38. Moderately stringent conditions "are defined as approximately 25° C. below the melting temperature of a perfectly base-paired double-stranded DNA . . . ." '332 patent, 1:42-45. Non-stringent hybridization conditions "are defined as approximately 35° C. or more below the melting temperature of a perfectly base-paired double-stranded DNA. . . . ." '332 patent, 3:59-61.

[38] In its brief, Digene cites the '332 patent, 2:66-3:2, as demonstrating that the epidemiological distribution test "requires satisfaction of two elements: (1) two HPV types must show substantially the same epidemiological distribution of cross-hybridization among genital lesions and (2) the DNA of the two HPV type must both cross-hybridize *under stringent conditions* with the same genital lesions, that comprise that epidemiological distribution." D.I. 438 at 14 (emphasis added). The italicized portion of that quotation is not part of, nor suggested by, the citation to which Digene directs the court.

[39] '332 patent, 15:41-16-11 (emphasis added).

HPV 35 clones 2A and 2B was employed.)[40]

Although Digene relies on the recitation of this particular test to support its proposed construction, the language cited is from part of the specification titled "EXAMPLE," which section is immediately preceded by the statement that "[t]he following example is given to further illustrate the present invention and is no way intended to limit the scope of the present invention."[41] After the specification recites particular test results, it is reiterated that "[w]hile this invention has been described in detail and with reference to *specific embodiments* thereof, it will be apparent to one skilled in the art that *various changes and modifications could be made therein without departing from the spirit and scope thereof.*"[42] Further, the specification discusses "the detection of HPV 35 DNA or RNA . . . based upon a comparison of epidemiological distribution of cross-hybridization" at other than stringent conditions.

> In the embodiment of the present invention wherein the detection of HPV 35 DNA or RNA is based upon a comparison of the epidemiological distribution of cross hybridization of an unknown sample of DNA or RNA . . . the unknown sample of DNA or RNA may exhibit less than 50% cross-hybridization with HPV 35 DNA under *moderately stringent hybridization conditions*, i.e., using hydroxyapatite chromatography for determining whether two HPVs represent different isolates of a common type or represent isolates of a different type, yet, may still be considered HPV 35 DNA or RNA *by the definitions herein*.[43]

Unlike the definition of the liquid hybridization test, which is defined as being

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[40] '332 patent, 16:30-34 (emphasis added).

[41] '332 patent, 12:17-19; '331 patent, 12:12-14 (same).

[42] '332 patent, 17:25-29 (emphasis added); '331 patent 17:9-13 (same).

[43] '332 patent, 11:8-20 (emphasis added).

conducted "under moderately stringent hybridization conditions,"[44] the epidemiological distribution test is defined as "show[ing] substantially the same epidemiological distribution of cross-hybridization among genital lesions and they both cross-hybridize with the same genital lesions which comprise the epidemiological distribution."[45] The court declines to add the limitation "under stringent conditions" found in a preferred embodiment to which the specification expressly states the invention is not limited.

Consequently, the court adopts Ventana's proposed construction:

An HPV where its DNA or RNA and ATCC Nos. 40330-40331:

(1) cross-hybridize to greater than 50%, as measured by hybridization in solution under moderately stringent hybridization conditions, or

(2) show substantially the same epidemiological distribution of cross-hybridization among genital lesions and cross-hybridize with the same genital lesions which comprise the epidemiological distribution.

2. "HPV 44" ('331 patent)

Digene's proposed construction is:

(1) an HPV whose DNA hybridizes to greater than 50% to the HPV DNA in clone 2 under moderately stringent conditions or

(2) and HPV whose DNA shows substantially the same epidemiological distribution of cross-hybridization among genital lesions as HPV 44 and that cross-hybridize under stringent conditions with the same genital lesions which comprise the HPV 44 epidemiological distribution.[46]

Ventana's proposed construction is:

An HPV where its DNA or RNA and ATCC No. 40353:

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[44] '332 patent, 1:42-43.

[45] '332 patent, 2:66-3-2.

[46] D.I. 440, Ex. F.

(1) cross-hybridize to greater than 50%, as measured by hybridization in solution under moderately stringent hybridization conditions, or

(2) show substantially the same epidemiological distribution of cross-hybridization among genital lesions and cross-hybridize with the same genital lesions which comprise the epidemiological distribution.[47]

For the same reasons set forth with respect to "HPV 35," the court adopts Ventana's construction.

3. "fragments thereof" ('331 and '332 patent)

Digene's proposed construction is: "a portion of DNA that is unique to HPV type 35 and no other HPV type as shown by its ability to hybridize to HPV 35 and not HPV types 1-34 when tested under stringent hybridization conditions"; "a portion of DNA that is unique to HPV type 44 and no other HPV type as shown by its ability to hybridize to HPV 44 and no other HPV type as shown by its ability to hybridize to HPV 44 and not HPV types 1-43 when tested under stringent [hybridization] conditions."[48]

Ventana's proposed construction is: "[a]ny sequence found within a larger piece of DNA or RNA and which may be as small as about 15 bases or base pairs in length."[49]

The court adopts Ventana's proposed construction.

The ordinary meaning of fragment is a small piece taken from a larger entity.[50] The specification states that "[t]he size of the HPV 35 DNA or HPV 35 RNA fragments

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[47] D.I. 439 at 9.

[48] D.I. 438 at 18, 18 n. 8.

[49] D.I. 439.

[50] *See* D.I. 439 at 10.

can be, for example, from about 15 to about 8000 bases . . . ."[51] and the parties are in agreement that the claim term "fragments thereof" refer to strands of DNA or RNA that are smaller than the approximately 8000 bases which make up HPV 35 or 44.[52] The parties' disagreement is whether "fragments thereof" must be defined to mean fragments of HPV 35 or 44 DNA or RNA which are unique to each of those HPVs.

Digene argues that the definition of the term "fragments thereof" as used in context of the claims of the patents-in-suit means a portion of HPV 35 DNA ('332 patent), or HPV 44 DNA ('331 patent), that is unique to that HPV type as shown by its ability to hybridize to that HPV type and not to other HPV types when tested under stringent conditions. Digene reasons that if a portion of DNA from a particular HPV type, e.g., HPV 35, cross-hybridizes with other HPV types, e.g., HPV types 1-34 under stringent conditions, then that fragment is not specific to HPV 35 and would not be a fragment of HPV 35. Digene's argues that its proposed construction is mandated to fulfill "the purpose and goal of the invention - - - namely to provide a HPV probe and/or method of using probes to specifically detect HPV 35."[53]

Ventana's proposed definition is not limited to sequences of DNA which are unique to HPV 35 or HPV 44. Ventana argues that neither the claims of the patents-in-suit nor the specification require that "fragments thereof" be construed to be fragments which are unique to HPV 35 or HPV 45 and that had the inventors wished to so limit

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[51] '332 patent 11:60-62.

[52] *See* D.I. 457 at 1 ("Both Digene and Ventana agree that 'fragments thereof' refers to strands of DNA that are smaller than the approximately 8000 bases which make up the HPV 35 and 44 genomes.").

[53] D.I. 438 at 18.

their claims they could have included that limiting language.

First, the court disagrees with Digene's implied proposition that the sole purpose of using HPV 35 probes is "to provide a HPV probe and/or method of using probes to specifically detect HPV 35." Digene is correct that the patent specification states that "under stringent hybridization conditions, HPV 35 DNA *or fragments thereof* or HPV 35 RNA *or fragments thereof* can be employed as probes for HPV 35 DNA or RNA *in particular*."[54] Immediately prior to that language, however, the specification also states that under non-stringent hybridization conditions, HPV 35 DNA *or fragments thereof* or HPV 35 RNA *or fragments thereof* can be employed as hybridization probes for HPV DNA or RNA *in general*[,]"[55] i.e., HPVs of types other than HPV 35 (or HPV 44 in the case of the '331 patent).

Moreover, the specification describes two ways that fragments of HPV 35 or HPV 44 may be obtained:

> The HPV 35 DNA fragments can be obtained by restriction endonuclease digestion of the HPV 35 clones 2A and 2B or by synthetically manufacturing such using any of the commercially available DNA synthesizing apparatus or by well known chemical methods using the HPV 35 DNA sequence which can be determined by well known means.[56]

The specification also recites: "HPV 35 DNA in its entirety can be excised from HPV clones 2A and 2B using BamHI restriction endonuclease and subcloned in any

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[54] '332 patent, 7:43-46 (emphasis added).

[55] '332 patent, 7:38-42 (emphasis added).

[56] '332 patent, 12:6-12; '331 patent 11:55-58; *see also* '332 patent, 6:64-69 ("The cloning of HPV 35 DNA or *fragments thereof* allows for the relatively simple production of large amounts of HPV 35 DNA *or fragments thereof* for use in the preparation of nucleic acid hybridization probes for HPV DNA or RNA *in general* and HPV 35 DNA or RNA *in particular*.") (emphasis added).

well known procaryotic and eucaryotic cloning vectors."[57] "*Fragments of* HPV 35 DNA can similarly be excised from HPV 35 clones 2A and 2B using other well known restriction endonucleases and cloned in the above described cloning vectors."[58]

In discussing obtaining fragments of HPV 35, the specification nowhere recites the need for those fragments to be made up of bases *unique* to HPV 35. Moreover, the inventor's knowledge that HPV 35 fragments may not be made up of unique bases is implied by the specification statement that "[w]hen detecting HPV 35 DNA or RNA, it is preferable to use *substantially all* of the HPV 35 genome as a hybridization probe."[59] Logically, a fragment that contains substantially all of the HPV 35 genome likely contains a unique sequence of bases to that HPV type, thereby making it preferable for detecting HPV 35 DNA or RNA in particular.

Because Ventana's proposed construction is consistent with the specification (which also does not suggest that a unique sequence is required) and would not subvert the purposes of the invention, the court adopts its proposed construction: any sequence found within a larger piece of DNA or RNA and which may be as small as about 15 bases or base pairs in length.

UNITED STATES MAGISTRATE JUDGE

[57] '332 patent, 6:41-44.

[58] '332 patent, 6:56-59 (emphasis added).

[59] '332 patent, 12:13-15 (emphasis added).