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Filed: January 16, 2015

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

JEREMY CLARK
Junior Party
(Application No. 11/854,218)

v.

RICHARD STORER, GILLES GOSSELIN, JEAN-PIERRE SOMMADOSSI, and PAOLA LACOLLA
Senior Party
(US 7,608,600 B2)

Interference No. 105,981 (JGN)
Technology Center 1600

Decision on Motions - Bd.R. 125

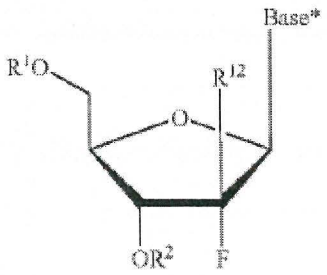
Before RICHARD E. SCHAFER, DEBORAH KATZ, and JOHN G. NEW, *Administrative Patent Judges.*

NEW, *Administrative Patent Judge.*

I. INTRODUCTION

This interference is before a merits panel for a decision on non-priority motions. The interference involves Junior Party Jeremy Clark's ("Clark") US Appl. No. 11/854,218 (the "'218 application") and Senior Party Richard Storer, Gilles Gosselin, Jean-Pierre Sommadossi, and Paola LaColla's ("Storer") US Patent 7,608,600 B2 (the "'600 patent"). Declaration at 1.[1] The subject matter of the interference is generally related to a method of using a class of 2′-fluoro, 2′-methyl (or halomethyl) nucleosides with a uracil or cytosine base for the treatment of a host infected with the hepatitis C virus ("HCV"). An important aspect of the nucleosides is the position of the fluorine moiety (F) in the "down" position as shown in the image below. Count 1 of the interference is Storer claim 1 or Clark claim 164 and recites:

> 1. A method for the treatment of a host infected with a hepatitis C virus, comprising administering to the host infected with a hepatitis C virus an effective amount of a compound having the formula:



> or a pharmaceutically acceptable salt thereof, wherein:

[1] Paper No. 1

R^1 is H; mono-, di- or triphosphate; acyl; an amino acid ester; a carbohydrate; a peptide;

or a pharmaceutically acceptable leaving group which when administered *in vivo* provides a compound wherein R^1 is H or phosphate;

R^2 is H; acyl; an amino acid ester; a carbohydrate; a peptide; or a pharmaceutically acceptable leaving group which when administered *in vivo* provides a compound wherein R^2 is H;

Base* is selected from the group consisting of adenine, N^6-alkylpurine, N^6-acylpurine, N^6-benzylpurine, N^6-halopurine, N^6-vinylpurine, N^6-acetylenic purine, N^6-acyl purine, N^6-hydroxyalkyl purine, N^6-alkylaminopurine, N^6-thioalkyl purine, N^2-alkylpurine, N^2-alkyl-6-thiopurine, thymine, cytosine, 5-fluorocytosine, 5-methylcytosine, 6-azapyrimidine, 6-azacytosine, 2- and/or 4-mercaptopyrimidine, uracil, 5-halouracil, 5-fluorouracil, C^5-alkylpyrimidine, C^5-benzylpyrimidine, C^5-halopyrimidine, C^5-vinylpyrimidine, C^5-acetylenic pyrimidine, C^5-acyl pyrimidine, C^5-hydroxyalkyl purine, C^5-amidopyrimidine, C^5-cyanopyrimidine, C^5-iodopyrimidine, C^6-iodo-pyrimidine, C^5-Br-vinyl pyrimidine, C^6-Br-vinyl pyrimidine, C^5-nitropyrimidine, C^6-amino-pyrimidine, N^2-alkylpurine, N^2-alkyl-6-thiopurine, 5-azacytidinyl, 5-azauracilyl, triazolopyridinyl, imidazolopyridinyl, pyrrolopyrimidinyl, pyrazolopyrimidinyl, guanine, hypoxanthine, 2,6-diaminopurine, and 6-choropurine;

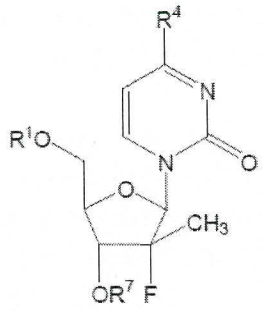
R^{12} is $C(Y^3)_3$; and

Y^3 is independently H or F.

or

164. A method for the treatment of hepatitis C infection, which comprises:

administering to a mammal in need thereof an antivirally effective amount of a (2′R)-2′-deoxy-2′-fluoro-2′-C-methyl nucleoside (β-D or β-L) or its pharmaceutically acceptable salt of the structure:



wherein R^1 and R^7 are independently H, a monophosphate, a diphosphate, a triphosphate, a H-phosphonate, an alkyl, an alkyl sulfonyl, or an arylalkyl sulfonyl; and

R^4 is NH_2 or OH.

Declaration at 3.

Before us are the following motions:

1. Clark Substantive Motion 1[2] to deprive Storer of the benefit of its US Appl. No. 60/392,350.

2. Clark Substantive Motion 2[3] to deprive Storer of the benefit accorded with respect to Count 1 of its U.S. Appl. No. 60/466,194.

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[2] Paper No. 389
[3] Paper No. 390

3. Clark Substantive Motion 3[4] to deprive Storer of the benefit accorded with respect to Count 1 of its U.S. Appl. No. 60/470,949.

4. Clark Substantive Motion 10[5] to deprive Storer of the benefit accorded with respect to Count 1 of US Appl. No. 10/6018,907.

5. Clark Substantive Motion 7[6] for judgment against Storer's US Patent No. 7,608,600 B2 on the grounds of unpatentability under 35 U.S.C. § 112, 1st paragraph, for lack of enablement and written description.

6. Clark Substantive Motion 5[7] to substitute Clark's proposed count 2 or, alternatively, Clark's proposed count 3, for Count 1.

7. Clark Substantive Motion 8[8] for judgment against Storer's US Patent No. 7,608,600 B2 on the ground of unpatentability under 35 U.S.C. § 101, for lack of utility and, accordingly, under 35 U.S.C. § 112, 1st paragraph, for lack of enablement.

8. Clark Substantive Motion 9[9] for judgment against Storer's US Patent No. 7,608,600 B2 on the ground of unpatentability under 35 U.S.C. §§ 102(e) or 103 as being either anticipated by, or obvious over, Clark's US Appl. No. 10/828,753.

9. Clark Miscellaneous Motion 18[10] to exclude evidence.

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[4] Paper No. 391
[5] Paper No. 392
[6] Paper No. 154
[7] Paper No. 162
[8] Paper No. 155
[9] Paper No. 156
[10] Paper No. 427

10. Storer Substantive Motion 5[11] to substitute proposed count B for Count 1.

11. Storer Substantive Motion 11[12] for judgment against Clark on the grounds of unpatentability of all of Clark's involved claims as anticipated under 35 U.S.C. § 102(e) and/or 103.

12. Storer Contingent Motion 14[13] to add a new claim to the interference.

13. Storer Contingent Motion 15[14] to add an application to the interference.

14. Storer Miscellaneous Motion 16[15] to exclude evidence.

We address these motions in the order presented above.

[11] Paper No. 157
[12] Paper No. 158
[13] Paper No. 327
[14] Paper No. 328
[15] Paper No. 425

II. CLARK MOTIONS

A. Clark Substantive Motion 1[16]

Clark Substantive Motion 1 seeks to deny Storer benefit for Count 1 of its US Appl. No. 60/392,350, filed June 28, 2002 (the "S1" application) pursuant to 37 C.F.R. § 41.208(3). Clark Subs. Motion 1, Paper 389 at 1. As challenger of Storer's accorded benefit, Clark must demonstrate that the S1 application does not constitute a constructive reduction to practice of Count 1. Bd.R. 42.201; SO ¶ 208.4.2. Clark argues that the S1 application does not describe, enable or provide a credible utility of any of the 2′-fluoro-2′-methyl nucleosides that constitute the subject matter of Count 1.

1. Enablement of the compounds of Count 1

The first paragraph of 35 U.S.C. § 112 requires that the specification of a patent must enable a person skilled in the art to make and use the claimed invention. *In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988). However, a patent

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[16] In addition to Clark's arguments set forth in the main body of this decision, Clark continues to argue that, despite the panel's prior decision (*see* Paper No. 350), interference estoppel should apply in this interference and that the Board should therefore reject Storer's attempts to argue issues that Storer raised, or could have raised, in the '871 interference. Motion at 8-9. Clark's attention is directed to the Federal Circuit's recent decision in *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1296-97 (Fed. Cir. 2014), holding that, because an interference action under 35 U.S.C. § 146 was pending in the district court, the Board's decision lacked requisite finality for purposes of estoppel. We therefore decline to address this argument further.

need not disclose what is already well known in the art at the time of invention. *See Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463 (Fed. Cir. 1984).

Clark seeks relief on the basis that Storer's S1 application does not constitute a constructive reduction to practice of the subject matter of Count 1, i.e., it does not include a described and enabled anticipatory embodiment that falls within Count 1. Count 1 is recited *supra*, and relates to methods of treating HCV infections with members of a genus of nucleosides, all of which possess a fluorine atom at the "down" position of the 2′ carbon atom on the ribose ring. Both parties agree that the S1 application provides no explicit disclosure or example of how such an embodiment of Count 1 can be synthesized. *See* Clark Subs. Motion 1, Paper 389 at 12; Storer Opp. 1, Paper 402 at 12; *see also* Ex. 1194, pp. 97-99, 101, 110, 121-122, 130. Failure to synthesize a single embodiment of the compounds recited in Count 1 would effectively prevent practice of the methods recited in the S1 application.

The question therefore devolves onto whether Clark, as challenger, can show, by a preponderance of the evidence, that a person skilled in the art, upon reading the Specification of the S1 application, and being knowledgeable concerning the prior art in the field of nucleoside synthesis, would not have been able to synthesize the 2′-fluoro ("down") nucleosides of Count 1 without undue experimentation. *See Wands*, 858 F.2d at 736-37; *see also Alcon Research Ltd. v. Barr Laboratories, Inc.*, 745 F.3d 1180, 1188 (Fed. Cir. 2014).

Whether synthesis would require undue experimentation is a "conclusion reached by weighing many factual considerations.... includ[ing] (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims"). *In re Wands*, 858 F.2d 731, 737 (Fed.Cir.1988).

With respect to the first *Wands* factor, the quantity of experimentation necessary for a skilled artisan to arrive at the invention, Clark argues that an artisan attempting to synthesize a compound recited in Count 1 would have been required to engage in an extensive and undue amount of experimentation. Clark Subs. Motion 1, Paper 389 at 15 (citing Ex. 2001, ¶¶ 167-176, 186, 202, 214, 229-231, 235, 248-250; Ex. 2044, p. 1; Ex. 2145, ¶¶ 85-101).

Clark points to the findings of the panel in the related 105,871 interference, which found that the Idenix team members had diligently attempted to make a 2′-fluoro-2′-methyl nucleoside as a high priority target for several years. Clark Subs. Motion 1, Paper 389 at 11. Clark observes that, during this interval, the Idenix team members were employed as chemists, several of whom hold doctoral degrees, but were nevertheless uniformly unsuccessful in synthesizing the target nucleoside. *Id.* Furthermore, argues Clark, Idenix also consulted outside experts, including individuals to whom Dr. Richard Storer, one of the Senior Party, referred to as an "expert in organofluorine chemistry" and a "world expert in carbohydrate chemistry" for advice on how to make a 2′-fluoro-2′-methyl nucleoside. However,

argues Clark, Storer alleged it was successful only after Clark's C2 application was published and Idenix scientists followed a procedure described therein. Clark Subs. Motion 1, Paper 389 at 15-16. Furthermore, argues Clark, documents produced by Storer show that Idenix chemists and/or consultants tried or considered trying numerous different fluorinating reagents when unsuccessfully attempting to synthesize a 2′-fluoro-2′-methyl nucleoside during the interval 2002-2005. Clark Subs. Motion 1, Paper 389 at 11.

Clark rejects the argument of Storer, and its technical expert Dr. Masad J. Damha,[17] that one skilled in the art as of June 28, 2002 would "immediately see," based on the prior art, that the fluorinating reagent N, N-Diethylaminosulfur trifluoride (Et_2NSF_3 or "DAST") could be readily used to make a 2′-fluoro-2′-methyl nucleoside from a nucleoside substituted at the 2′ position with a tertiary alcohol (OH) because DAST was a well-known and predictable reagent for fluorinating nucleosides, including those with tertiary alcohols at the 2′ position. Clark Subs. Motion 1, Paper 389 at 10 (citing Storer Substantive Motion 5, pp. 18-

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[17] Storer's expert witness is Dr. Masad J. Damha. Dr. Damha is currently James McGill Professor of Chemistry at McGill University, Montreal, Canada, where he has been a faculty member since 1992. Ex. 1132, ¶ 2. He has also received a number of distinguished awards and is the author of approximately 150 papers and book chapters in peer-reviewed journals, many of which address the synthesis of nucleoside analogs. *Id.*, ¶ 7. Dr. Damha has also consulted for pharmaceutical companies in the United States and Canada and has presented lectures and conference presentations at academia and industry on synthesis and applications of nucleosides, oligonucleotides and their analogs. *Id.*, ¶ 9. Upon review of his curriculum vitae, we find that Dr. Damha is therefore qualified to opine as an expert on the subject matter of this interference.

20, ll. 11-3; Storer Contingent Responsive Motion 14, p. 18-19, ll. 6-16; Ex. 1132,[18] ¶¶ 64, 69-76). Clark points out that Dr. Damha admitted, on cross-examination, that none of the references on which he relied for this contention actually show fluorination of a tertiary alcohol at a nucleoside's 2′ position using DAST. *Id.* (citing Ex. 1194, p. 125, ll. 4-18; Ex. 2145,[19] ¶ 96; Ex. 1148,[20] pp. 10761-10770; Ex. 1160,[21] pp. 65-96; Ex. 1161,[22] pp. 574-578).

Storer argues that the S1 application provides precursor molecules and guidance that would have enabled one skilled in the art to synthesize a 2′-methyl ("up") 2′-fluoro ("down") nucleoside without undue experimentation. Storer Opp. 1, Paper 402 at 4-5. Storer points to compound 17 of Exhibit 1140, Akira Matsuda et al., *Alkyl addition reaction of pyrimidine 2′-Ketonucleosides: Synthesis of 2′-Branched-Chain Sugar Pyrimidine Nucleosides (Nucleosides and Nucleotides. LXXXI)*, 36(3) CHEM. PHARM. BULL. 945-953 (1988) ("Matsuda"). Storer contends that a skilled artisan would have recognized that compound 17 of Exhibit 1140 was a precursor to the claimed compound. *Id.* at 4-5 (citing Ex. 1200, ¶ 91; Ex. 2139, at 110-112, ll. 25-7; Ex. 1144, p 949; Ex. 2001, ¶ 323). Compound 17 of Matsuda is reproduced below:

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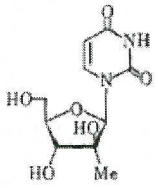
[18] Paper No. 679
[19] Paper No. 400
[20] Paper No. 345
[21] Paper No. 309
[22] Paper No. 310



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Compound 17 of Matsuda depicts 2′-hydroxy-2′-methyl cytidine

Storer argues that a skilled artisan, when looking at the structure of the claimed compound, would necessarily have recognized the need for a fluorinating reagent for synthesis and that replacement of a hydroxyl (OH) group with fluorine (deoxyfluorination) was a well-known organic transformation, as cited in such reference texts such as Richard C. Larock, COMPREHENSIVE ORGANIC TRANSFORMATIONS: A GUIDE TO FUNCTIONAL GROUP PREPARATIONS (2nd ed.) (1999) ("Larock 1999") (Ex. 1199). Storer Opp. 1, Paper 402 at 5 (citing Ex. 1200, ¶ 89; Ex. 2139, p. 100-101, ll. 22-15; Ex. 1248,[23] p. 90, ll. 13-19, p. 91, ll. 14-21, Ex. 1200, ¶ 79; Ex. 2139, p. 127, ll. 4-7; Ex. 1199, at 689 to 690 (Chapter 8, "Halogenation of Alcohols")).

Storer also points out that Larock teaches the use of DAST in the deoxyfluorination of a "variety of chemical compounds with success" and argues that, by 2002, DAST was known as "the most convenient and powerful reagent for deoxyfluorination" reactions.[24] Storer Opp. 1, Paper 402 at 5-6 (citing Ex. 2014, p.

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[23] Paper No. 549

[24] DAST is a nucleophilic fluorinating agent and acts by displacing the hydroxyl group and inverting the position of the methyl group. Thus, a 2′-hydroxy ("up") –

259; Ex. 1200, ¶ 82; Ex. 1223,[25] p. 2357; Ex. 2139, pp. 126-127, ll. 17-3). Therefore, argues Storer, a skilled artisan would have appreciated that DAST could have been used to transform the hydroxyl group of known nucleosides, such as Matsuda Compound 17, into the 2′ ("down") fluorinated nucleosides recited in Count 1. *Id.* at 6 (citing Ex. 1200, ¶ 85). Accordingly, contends Storer, the prior art disclosed information that would have enabled a skilled artisan to synthesize a 2′-methyl ("up") 2′-fluoro ("down") nucleoside within the scope of Count 1. *Id.* (citing Ex. 1200, ¶¶.74-99).

By way of example, Storer points out that an Idenix scientist, Jingyang Wang, synthesized the compound, using DAST, on her first attempt without the benefit of Clark's publication. Storer Opp. 1, Paper 402 at 6 (citing Ex 1232,[26] ¶¶ 17-20; Ex. 1233,[27] p. 70, ll. 5-11; *see also* Ex. 1231[28]). Storer argues that is also informative that Clark, a chemist without a Ph.D., was allegedly able to make a 2′-methyl (up)-2′-fluoro (down) nucleoside in just a few months using DAST. *Id.* (citing Ex. 1246,[29] p. 40, ll. 2-3; Ex. 1247,[30] ¶¶ 32, 39, 41).

2′ methyl ("down") cyclic sugar may become a 2′-methyl ("up") -2′-fluoro ("down") cyclic sugar. *See, e.g.*, Ex. 2014.

[25] Paper No. 527
[26] Paper No. 535
[27] Paper No. 536
[28] Paper No. 534
[29] Paper No. 547
[30] Paper No. 548

Consequently, argues Storer, the synthesis of a 2′-fluoro-2′-methyl nucleoside would not have required undue experimentation by one skilled in the art.

We find it informative that Idenix's research team in Montpellier, France, repeatedly attempted without success to synthesize a 2′-methyl ("up") 2′-fluoro ("down") nucleoside during the interval between December, 2002 and September, 2004. *See, generally*, Ex. 2128; 2129. Regular progress reports and correspondence of the Montpellier team during this interval demonstrate that synthesis of a 2′-fluoro-2′-methyl nucleoside during this interval was considered to be a high-priority result. Exs. 2026-2044; *see, e.g.*, Ex. 2037, p. 3 (report dated July, 31, 2003: stating that synthesis of a 2′-fluoro-2′-methyl nucleoside with the fluoro substituent in the "down" position "still a high priority").

During this interval, Idenix scientists also corresponded with consultants Dr. George Fleet and Dr. Paul Coe in an attempt to effect a synthesis of the desired compound. *See, e.g.*, Ex. 2034[31] ("Prioritized Summary of Idenix Meeting with G.W. J. Fleet held on 10th May 2004"); Ex. 2038 (communication from Dr. Coe to Dr. Storer entitled "Thoughts on your synthesis problems"). Dr. Richard Storer, one of the inventors of the S1 application, describes Dr. Fleet as "an expert in carbohydrate chemistry" and "one of the best in the world" and describes Dr. Coe as "an expert in organofluorine chemistry." Ex. 2131[32], pp. 35, 74. Both consultants suggested possible schemes for the synthesis of a 2′-fluoro-2′-methyl

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[31] Paper No. 74
[32] Paper No. 625

nucleoside with the fluorine substituent in the "down" position. Ex. 2034; Ex. 2038. In the latter communication, Dr. Coe related that:

> [I]n our experience and indeed in that of manner [sic] other[,] particularly the de Clerc group[,] the most viable routes to fluoro nucleosides are by sugar/base condensation methods the anomer problem notwithstanding, for the very reasons you have discovered, in that leaving groups generated in situ[,] e.g.[,] in DAST reactions are readily attacked by the pyrimidine ring nucleophiles or elimination and/or participation of the blocking groups. Further migrations of groups can readily occur.

Ex. 2038, p. 1.

Idenix personnel also attended a "Scientific Update Course" entitled "Making and Using Fluoroorganic Molecules" in April, 2003, and submitted a report summarizing the course content. Ex. 2039.

Nevertheless, despite these consultations, the Montpellier team was never able to successfully synthesize a 2′-fluoro-2′-methyl nucleoside with the fluorine substituent in the "down" position. Dr. Jean-François Griffon,[33] leader of the Montpellier group, testified that he attempted at least seven different synthetic schemes, including several suggested by Dr. Coe, and in some cases employing DAST, without success. Ex. 2128, ¶¶ 8-64; Ex. 2132, p. 57. As Dr. Griffon reported in an email to Dr. Storer on March 4, 2003: "As I told you last week at the end of the Summary Meeting, the compound I obtained after treatment with

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[33] By the standard we determined *infra*, we find that Dr. Griffon qualifies as a person skilled in the art. *See* Ex. 2152 (Paper No. 542).

DeoxoFluor[34] and deprotection was not the (very!) expected Fluoro derivative but the 2′-methylene derivative." Ex. 2029, p. 1. A diagram in the accompanying report documents the failure of this synthetic scheme, the end product having a 2′-methylene group rather than the desired 2′-methyl-2′-fluoro groups:

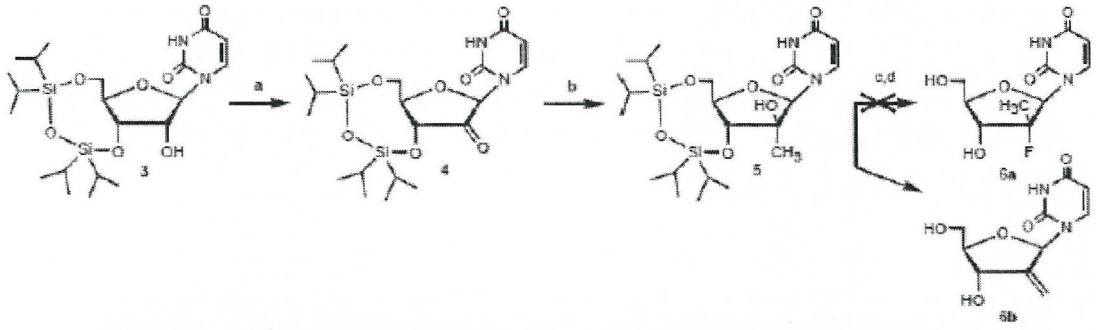

Illustration from Ex. 2029 indicating synthesis of an undesired 2′-methylene nucleoside (6b) rather than a 2′ (down) fluorination (6a).

Id., p. 3

Furthermore, attempts by the Montpellier team to use DAST in the synthesis of a 2′-fluoro-2′-methyl nucleoside produced similar failures, as this diagram from an Idenix summary of results indicates:

[34] Deoxo-Fluor® is, like DAST, a nucleophilic organic fluorinating agent. *See, e.g.,* R.P. Singh and M.S. Jean'ne, *Recent advances in nucleophilic fluorination reactions of organic compounds using deoxofluor and DAST*, 17 SYNTHESIS 2561-2578 (2002).

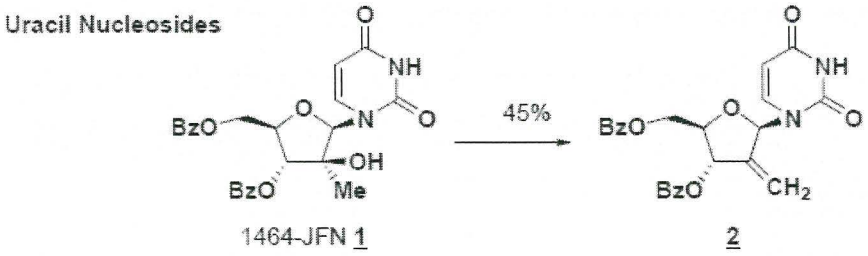

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Illustration from Ex. 2041 indicating synthesis of an undesired 2′-methylene nucleoside via DAST reaction.

Ex. 2041, p. 2. The difficulties experienced by Idenix in synthesizing a 2′-fluoro-2′-methyl nucleoside are expressed in a November 11, 2014 email from Dr. Storer stating:

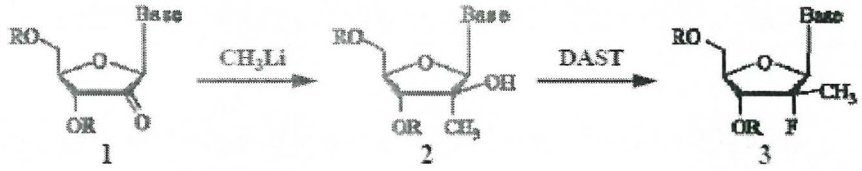
> When we get this information together we'll decide what, if anything, we will do in house and how it it [sic] fits with what anyone else knows. *A lot of things which look simple on paper in related systems have been tried and don't work in this series. Having to make the tertiary fluoride is very different to having to make a secondary.*

Ex. 2044, p. 1 (emphasis added).

With respect to the testimony of Jingyang Wang who allegedly synthesized the desired compound in a single attempt in January, 2015, at Idenix's research facility in Cambridge, Massachusetts, we note that, prior to beginning her synthesis, Ms. Wang had received the reports from the Montpellier group as well as intermediate compositions synthesized at Montpellier. Ex. 1233, pp. 99-101. Consequently, Ms. Wang was not, as Storer seems to suggest, attempting synthesis of a 2′-fluoro-2′-methyl nucleoside *ab initio*, but rather had the hindsight benefit of the Montpellier group's efforts. *Id.*

Similarly, Storer's expert, Dr. Damha, points in his Declaration to what he terms Scheme A, of which the first step is disclosed by the S1 application. Ex. 1132, ¶ 67; *see also* Ex. 1003, p. 120. Scheme A of Dr. Damha's declaration is reproduced below:

Scheme A



Scheme A shows a sequence of two steps by which a 2′-keto group is replaced by a 2′-hydroxyl (up) - 2′-methyl (down) nucleoside which is in turn replaced by DAST with a 2′-methyl (up)-2′-fluoro (down) nucleoside.

Ex. 1132, ¶ 67. The intermediate form 2 in Scheme A also corresponds to Matsuda compound 17. *Id.*, ¶ 69, fn. 5. According to Dr. Damha:

> A person skilled in the art as of June 28, 2002 could therefore simply look at the 2′-F-2′-methyl-ribonucleoside species disclosed in the '350 Application, and synthesize it without undue experimentation using: (i) the starting materials and reagents disclosed in the '350 Application and known in the art [i.e., Matsuda compound 17], and (ii) the then-existing routine DAST chemistry. It is well known that all organic reactions produce by-product(s). As of June 28, 2002, it would not have been a surprise to a person skilled in the art that DAST fluorination might lead to elimination, rearrangement, or other by-products. However, just like all other organic reactions, the DAST fluorination does not need to be perfect to be useful in organic synthesis, as separation and purification techniques were well-known as a [sic] of June 2002.

Id., ¶ 76. However, Dr. Damha's opinion is not borne out by the fact that this very reaction was attempted by the Montpellier group and was not successful: attempts to fluorinate compound 17 with DAST yielded a 2′-methylene nucleoside. *See* Ex. 2041, p. 2. Such a result is supported by Dr. Coe's suggestion that "leaving groups generated in … DAST reactions are readily attacked by the pyrimidine ring nucleophiles or elimination and/or participation of the blocking groups." Ex. 2038, p. 1. The use of other fluorinating agents yielded similarly unsuccessful results. *See, e.g.,* Ex. 2029, p. 3 (using DeoxoFluor® as the fluorinating agent).

We therefore find, based upon the proffered evidence, that a high amount of experimentation is necessary to synthesize a 2′-fluoro-2′-methyl nucleoside with the fluoro moiety in the "down" position requiring at least two years of a high priority experimentation by persons skilled in the art, including multiple consultations with experts at the top of their fields and additional formal training.

With respect to the second *Wands* factor, the amount of direction or guidance presented, Clark argues, and Storer does not contest, that the S1 application provides no explicit explanation or example describing synthesis of a 2′-flouro "down" nucleoside as embodied in Count 1. *See* Clark Subs. Motion 1, Paper 389 12; Storer Opp. 1, Paper 402 at 12. Clark also argues that no synthesis of a 2′-fluoro-2′-$C(H/F)_3$ nucleoside, including any 2′-fluoro-2′-methyl nucleoside, had been reported in the available art as of the S1 application's June 28, 2002 filing date. Clark Subs. Motion 1, Paper 389 at 9 (citing Ex. 2001, ¶¶

137, 231; Ex. 2005, p. 22, ll. 4-8; Ex. 1194,[35] p. 91, ll. 12-16). Rather, argues Clark, its own US Appl. Pub. No. 2005/0009737 A1 (the "C2 application"), published on January 13, 2005 (subsequent to the S1 application's June 28, 2002 filing date), was the first reported synthesis of a 2′-fluoro-2′-methyl nucleoside, an embodiment of Count 1. *Id.* at 9-10 (citing Ex. 2001, ¶¶ 137, 162; Ex. 2003, ¶¶ 221, 222; Ex. 2005, p. 22, ll. 4-8; Ex. 2013,[36] cover page (item 43), ¶ [0294]-[0035]).

Furthermore, argues Clark, the S1 application's failure to disclose any specific starting materials or conditions under which such a compound could be made cannot be rectified by reliance on the prior art for all of the required teachings. *Id.* (citing *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997); also citing Ex 2005, pp. 24-25, ll. 13-10, 26, ll. 2-5). Clark contends that Storer and its expert, Dr. Damha, argue that the S1 application discloses "starting materials" and reagents (e.g., methyl lithium) for making 2′-fluoro-2′-methyl nucleosides, and that an artisan purportedly would have "immediately identified" operative methods for making such compounds by reacting DAST with a 2′-methyl-2′-hydroxy nucleoside. Clark Subs. Motion 1, Paper 389 at 13.

However, Clark relates, Dr. Damha, on cross-examination, admitted that: (1) no such methods are found in the S1 application; (2) the S1 application does not discuss any fluorinating reagents, including DAST; (3) the S1 application does not

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[35] Paper No. 498
[36] Paper No. 56

disclose intermediate Compound 2 and final Compound 3 shown in Dr. Damha's "Scheme A"; (4) nothing in Scheme 4 of the S1 application suggests isolating the intermediate Compound 2 needed for the Damha "Scheme A" route, which has a methyl group "down" and a hydroxyl group "up" at the 2′ position (the opposite 2′ stereochemistry from the compounds in Scheme 4); and (5) contrary to his declaration, the S1 application does not "explicitly disclose" the reagent methyl lithium. Clark Subs. Motion 1, Paper 389 at 14 (citing Ex. 1194, pp. 97, ll. 5-8, 98, ll. 11-17, 98-99, ll. 22-17, 101, ll. 15-16, 110, ll. 14-24, 121-122, ll. 19-11, 130, ll. 7-16).

Clark also argues that Dr. Damha's opinion relies on references not mentioned in the S1 application, and he did not consider whether the S1 application would have guided an artisan to such literature. Clark Subs. Motion 1, Paper 389 at 14 (citing Ex. 1194, pp. 102, ll.12-17, 133-135, ll. 24-2).

Storer responds that the S1 application provides adequate guidance for synthesizing compounds within Count 1. Storer Opp. 1, Paper 402 at 9-10. Storer argues that the fluorination reagent DAST was known to the skilled artisan for substituting fluorine for a hydroxyl group with inversion. *Id.* at 10. Therefore, argues Storer, recognizing that inversion will occur, a skilled artisan would have known to start with a nucleoside having a similar structure to that defined by Count 1, but with a 2′-OH (up) group, in order to obtain the desired 2′-F (down) structure of the compounds within Count 1. *Id.*at 12. (citing Ex. 1200, ¶ 90).

Storer points out that Clark's expert, Dr. Stanislaus Wnuk[37] agreed that a skilled artisan would have recognized Matsuda Compound 17 as a potential precursor to the subject matter of count 1, which is depicted at paragraph 323 of his Declaration. Storer Opp. 1, Paper 402 at 12 (citing Ex. 2001). Storer points out that Matsuda Compound 17 differs from the claimed compound in that the configuration at the 2′-position is inverted with a 2′-OH (up) instead of a 2′-fluoro (down). *Id.* at 12-13 (citing Ex. 1200, ¶ 92; Ex. 2139, pp. 107-108, ll. 18-6). Further, alleges Storer, both parties' experts agree that the synthesis of the compound of Count 1 would have been essentially a one-step reaction of Matsuda Compound 17 with DAST. *Id.* at 13 (citing Ex. 1200, ¶ 94; Ex. 2139, p. 156, ll. 2-12). Store contends that the synthesis of Matsuda Compound 17 is the same as the product of the first steps of Scheme 4 of the S1 application which is reproduced, in part, below:

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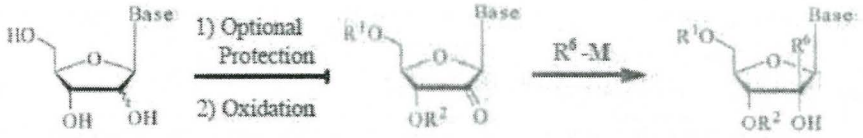
[37] Clark's expert witness, Dr. Stanislaus F. Wnuk received his Ph.D. in organic chemistry from Adam Mickiewicz University in Poznan, Poland in 1983 and is currently Professor of Chemistry at Florida International University, a position he has held since 1997. Ex. 2001, ¶¶ 8-9. He is the author of over 120 publications, more than 80 of which pertain to nucleosides or nucleotides, with approximately 30 of those relating to fluorinated nucleosides or nucleotides. *Id.*, ¶ 12. He has also received a number of research and teaching awards. *Id.*, ¶ 11. Upon review of his curriculum vitae, we find that Dr. Wnuk is sufficiently qualified as an expert to opine on the synthesis of fluorinated nucleosides.

Scheme 4



The initial reaction steps of Scheme 4 depicts synthesis of Compound 17 of Matsuda, where R^6 is methyl, R^1 and R^2 are protective groups, and the base is uracil

Id. (citing Ex 1132, ¶¶ 65, 66; Ex. 1003, p. 120). Storer points out that the intermediate compound (2′-keto) of Scheme 4 is the starting material of Matsuda Compound 17, wherein R^1 and R^2 form protecting groups and the Base is uracil. *Id.* (citing Ex. 1132, ¶¶ 65-66; Ex. 1003, p. 120; Ex 1144, pp. 945-953).

As such, contends Storer, the specification of the S1 application teaches the starting materials and methods for making Matsuda Compound 17, which is a precursor to the claimed compound. Storer Opp. 1, Paper 402 at 13. Storer concludes that the S1 application therefore provides a skilled artisan with the starting materials and guidance for making the compounds within Count 1 without undue experimentation. *Id.* (citing Ex. 1200, ¶ 97).

We agree with Clark that the S1 application provides no explicit explanation or guidance as to how to synthesize a 2′-flouro "down" nucleoside as embodied in Count 1. Moreover, we have related *supra* how the Idenix team identified such a molecule as a high-priority target, but failed to synthesize such a compound for approximately two years subsequent to the submission of the S1 application. Moreover, we have related how the Idenix team attempted the very syntheses that

Storer's expert Dr. Damha states would be suggested by the disclosures of the S1 document, but were unable to successfully synthesize the target molecule. We therefore find that the S1 application provides little in the way of direction or guidance as to how to synthesize a 2′-fluoro-2′-methyl nucleoside with the fluoro moiety in the "down" position.

The third *Wands* factor enquires into the presence or absence of working examples of the invention. It is uncontested by the parties that there were no examples of such a molecule reported in the art prior to submission of the S1 application. Clark Subs. Motion 1, Paper 389 at 9. Clark contends, and Storer does not contest, that the S1 application lacks a single, specific example teaching how to synthesize any nucleoside having a fluorine atom substituent on the ribose ring. Clark Subs. Motion 1, Paper 389 at 12-13 (citing Ex. 2001, ¶¶ 138, 186, 202, 214, 230, 249; Ex. 2049, pp. 1-5297, ll. 1-21, Figs. 1-4). Additionally, argues Clark, the S1 application lacks any working example that an artisan could have modified, without extensive experimentation, to make a compound falling within either of Count 1's chemical formulae. *Id.* at 13 (Ex. 2001, ¶¶ 138-141, 186, 202, 214, 229, 230, 235, 248, 249; Ex. 2049, pp. 1, ll.1-5297, Figs. 1-4; Ex. 2005, pp. 23-24, ll. 18-3).

With respect to the fourth *Wands* factor, the nature of the invention, Clark contends that Count 1 is directed to methods for treating HCV infection using certain 2′-fluoro-2′-C(H/F)$_3$ nucleosides, including certain 2′-fluoro-2′-methyl nucleosides. Clark Subs. Motion 1, Paper 389 at 9 (citing Ex. 2001, ¶¶ 45-50; Ex.

2003,[38] ¶¶ 26, 28, 31-33, 40-42; Ex 2012,[39] p. 2:8-17; Ex. 2098,[40] col. 2221, ll. 9-52). According to Clark, because such compounds were not commercially available as of June 28, 2002, it would have been necessary for an artisan to make a compound falling within one of Count 1's chemical formulae. *Id.* (citing Ex. 2001, ¶ 136; Ex. 2005, p. 20, ll. 23-26).

Storer does not contest Clark's characterization of the nature of the invention, but responds that the nature of the invention is such as to require a high level of skill in the art, so much so that a skilled artisan would have been familiar with the methods for synthesizing nucleosides of the type within Count 1.

We find that the nature of the invention, as recite in Count 1 is best characterized as the administration of a genus of nucleosides used in the treatment of viruses, particularly those of the family *Flaviviridae* (which includes HBV and HCV[41]). We also find that, as of the time of filing of the S1 application, although organic fluoridation mechanisms were generally well-known in the art a 2′-fluoro-2′-methyl nucleoside with the fluoro substituent in the "down" position had not yet been synthesized.

With respect to the fifth *Wands* factor, the state of the prior art, Clark argues that no synthesis of a 2′-fluoro-2′-C(H/F)$_3$ nucleoside, including any 2′-fluoro-2′-methyl nucleoside, had been reported in the available art as of S1's June 28, 2002 filing date. Clark Subs. Motion 1, Paper 389 at 9 (Ex. 2001, ¶¶ 137, 231; Ex.

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[38] Paper No. 47
[39] Paper No. 55
[40] Paper No. 137
[41] *See, e.g.*, Clark Subs. Motion 1, Paper 398 at 2

2005, p. 22, ll. 4-8; Ex. 1194,[42] p. 91, ll. 12-16). Rather, argues Clark, its US Appl. Pub. No. 2005/0009737 A1 (the "C2 application"), published on January 13, 2005 (subsequent to the S1 application's June 28, 2002 filing date), was the first reported synthesis of a 2′-fluoro-2′-methyl nucleoside. *Id.* at 9-10 (citing Ex. 2001, ¶¶ 137, 162; Ex. 2003, ¶¶ 221, 222; Ex. 2005, p. 22, ll. 4-8; Ex. 2013,[43] cover page (item 43), ¶ [0294]-[0035]).

Storer argues that the specification of the S1 application, when viewed in light of the prior art, discloses sufficient information to enable a skilled artisan to synthesize a 2′-methyl (up)-2′-F (down) nucleoside without undue experimentation. Storer Opp. 1, Paper 402 at 4. According to Storer, and as argued *supra*, a skilled artisan would have readily recognized that a well-known precursor to the nucleoside, such as Matsuda Compound 17, could have been transformed in a single step to a nucleoside within the scope of the count. *Id.* (citing Ex. 1132, ¶25; Ex. 1144,[44] p. 949; Ex 1115,[45] pp. 40-45). Storer argues that compounds that were one reaction step away from the compounds of Count 1, such as 2′-methyl (down)-2′-OH (up) nucleosides, were well known by June 2002. *Id.* (citing Ex. 1132, ¶ 25; Ex. 1144, p. 949; Ex. 1115, pp. 40-45).

Reviewing the evidence before us, we find, with respect to the prior art, that certain methods of organic fluoridation were well-known at the time of invention, but that synthesis of a 2′-fluoro-2′-methyl nucleoside had not yet been reported in

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[42] Paper No. 498
[43] Paper No. 56
[44] Paper No. 293
[45] Paper No. 269

the prior art. *See* Ex. 1132, ¶ 33. The fluorinating agent DAST was well-known in the prior art to be useful in the fluorination of nucleosides and nucleoside analogs. For example, Johanna Wachtmeister et al., *Synthesis of 4-substituted carbocyclic 2,3-dideoxy-3-C-hydroxymethyl nucleoside analogues as potential anti-viral agents*, 55 TETRAHEDRON 10761 (1999) ("Wachtmeister") teaches the use of DAST in the fluoridation of certain carbocyclic nucleoside analogs in which the oxygen in the five-member ribose ring is replaced with a carbon atom and fluoridation takes place at the C-4 position. Ex. 1148, p. 10763. Similarly, P. Herdewijn et al., *Synthesis of nucleosides fluorinated in the sugar moiety. The application of diethylaminosulfur trifluoride to the synthesis of fluorinated nucleosides*, 8(1) NUCLEOSIDES AND NUCLEOTIDES 65 (1989) ("Herdewijn") teaches using DAST for, *inter alia*, fluoridation of nucleosides at the 2′ position. Ex. 1160, pp. 65-96. A. Van Aerschot et al., *2′,3′-difluoro- and 3′-azido-2′-fluoro substituted dideoxypyrimidines as potential anti-HIV agents*, 98(12) BULL. SOC. CHIM. BELG. 937 (1989) ("Van Aerschot") teaches the use of DAST to produce various 2′-fluoro-nucleoside analogs. Ex. 1151,[46] pp. 938-941. Hiroyuki Hayakawa et al., *Diethylaminosulfur trifluoride (DAST) as a fluorinating agent of pyrimidine nucleosides having a 2′,3′-vicinal diol system*, 38(5) CHEM. PHARM. BULL. 1136 (1990) ("Hayakawa") teaches that although "participation of the base moiety often thwarts the desired introduction of a fluorine atom … appropriate modification of the base and/or sugar moieties allowed the desired fluorodehydroxylation to occur, giving 5′-, 3′-β, and 2′-α-fluorinated

[46] Paper No. 300

uracilnucleosides in good yields." Ex. 1152, p. 1136. Consequently, we find that it was well-known in the prior art that DAST could be employed in the 2′ fluoridation of nucleosides and nucleoside analogs.

Dr. Damha cites these prior art references, among others, as demonstrating that:

> The fluorinating reagent, DAST, may be used to prepare a 2′-F-ribonucleoside in a single step from an "arabinonucleoside" (compound 2 of Scheme A, above). As of June 28, 2002, DAST had routinely been used in the nucleoside field to install a fluoro group at the 2′-position of nucleosides, often with an unprotected nucleobase, in a single step under very mild conditions.

Ex. 1132, ¶ 71. However, Dr. Damha admits that none of these references teaches using DAST to convert a tertiary alcohol at a nucleoside 2′ position to a tertiary fluoride at the nucleoside 2′ position:

> Q. [Ms. Austin] I just want to make sure the record is clear. So just maybe a yes or a no, did any of these references describe using DAST to convert a tertiary alcohol at a nucleoside 2′ position to a tertiary fluoride at the nucleoside 2′ position?
>
> […]
>
> A. [Dr. Damha] No.

Ex. 1194, p. 125. And Dr. Wnuk opined in response that "I believe it is an oversimplification to assert that, because DAST had been used to fluorinate certain

secondary and tertiary alcohols[47] with inversion of stereochemistry, it was therefore well-known that it would react similarly with significantly different substrates." Ex. 2145, ¶ 96.

We consequently find, with respect to the fifth *Wands* factor, that although DAST was well-known in the prior art as fluoridating agent for nucleosides and nucleoside analogs, the prior art did not teach, or explicitly suggest, the use of DAST in the fluoridation of a tertiary alcohol to convert a tertiary alcohol at a nucleoside 2′ position to a tertiary fluorine at the nucleoside 2′ "down" position. We further find that, although organic fluoridation techniques were well-known in the art at the time the S1 application was filed, fluoridation of tertiary alcohols to produce a 2′ "down" tertiary fluorine was not taught or suggested by the prior art.

The sixth *Wands* factor is the relative level of skill of those in the art. The parties largely agree that the level of skill in the art is very high and on the

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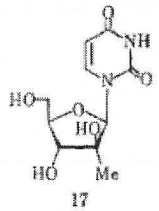
[47] In a secondary alcohol, the carbon atom binding the hydroxyl group is attached directly to two alkyl groups, which may be the same or different. In a tertiary alcohol, the carbon atom binding the hydroxyl group is attached directly to three alkyl groups, any combination of same or different. By way of example, Matsuda compound 17:



17

is a tertiary alcohol because the 2′ carbon binding the hydroxyl group is bound to three carbons: the 1′ and 3′ ring carbons and the carbon of the methyl (Me) group.

qualifications of a person of ordinary skill. *See* Ex. 1132, ¶ 14; Ex. 2001, ¶¶ 60-61. We therefore find that a person possessing the ordinary level of skill in this art, as of the time of invention, would hold a doctoral degree in the field of organic, synthetic, or medicinal chemistry with at least a year's experience in the field of nucleoside synthesis or relevant drug discovery. Alternatively, that artisan could hold a master's degree in one of those same fields with at least three years of practical experience in the field of nucleoside synthesis or relevant drug discovery.

With respect to the seventh *Wands* factor, the predictability or unpredictability of the art, Clark argues that the fluorination chemistry involved in attempting to synthesize 2′-fluoro ("down") 2′-C(H/F)$_3$ ("up") nucleosides was unpredictable at the time of Idenix's attempts to do so, because there was no precedent in the literature for making such a substitution on tertiary carbons of the ribose ring. Clark Subs. Motion 1, Paper 389 at 12 (citing Ex. 2001, ¶¶ 154-159, 231; Ex. 2005, p. 22, ll. 12-17, Ex. 2007, pp. 19, ll. 4-12, 22, ll. 5-18; Ex. 2022,[48] pp. 65-96; Ex. 2023,[49] pp. 574-78; Ex. 2024,[50] pp. 2315-16; Ex. 2025,[51] pp. 251-54; Ex. 1194, pp. 91, ll. 12-16, 92, ll. 3-93:18, 125, ll. 4-18). Clark maintains that the prior art demonstrated that attempted fluorination reactions (including those involving DAST) could fail, resulting in unfluorinated elimination and/or rearrangement products, or products with incorrect stereochemistry. *Id.* (citing Ex.

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[48] Paper No. 62
[49] Paper No. 63
[50] Paper No. 64
[51] Paper No. 65

2001, ¶¶ 156, 231; Ex. 2014,[52] p. 259, ll. 15-20; Ex. 2015,[53] pp. 7570-7571, ll. 18-4; Ex. 2016,[54] pp. 2563 (left col, ll. 11-14, Scheme 5), 2564 (Scheme 9); Ex. 2017,[55] pp. 1090-91; Ex. 2018,[56] pp. 554-55; Ex. 2139,[57] pp. 156-157, ll. 15-3).

Clark argues further that the documents that produced by Storer in the related 105,871 Interference demonstrate that DAST treatment of tertiary and secondary alcohols failed to produce fluorinated products. Clark points out that Dr. Paul Coe, an expert in organofluorines expressed skepticism regarding the use of DAST; and Dr. Richard Storer stated that "[a] lot of things which look simple on paper in related systems have been tried and don't work in this series. Having to make the tertiary fluoride is very different to [sic] having to make secondary." *Id.* (citing Ex. 2001, ¶¶ 157, 158, 174; Ex. 2007, pp. 15-17, ll. 15-2; 20, ll. 3-8; Ex. 2029, p. 2 (numbered p. 1); Ex. 2035, p. 3 (numbered p. 2); Ex. 2038, pp. 1-3, 5-10; Ex. 2041,[58] p. 1; Ex. 2042,[59] p. 1; Ex. 2043,[60] pp. 38, 40; Ex. 2044,[61] p. 1; Ex 2139, pp. 146, ll. 9-22, 147, ll. 14-23).

Storer responds that deoxyfluorination with DAST was highly predictable. Storer Opp. 1, Paper 402 at 7 (citing Ex. 1200, ¶¶ 100-131). According to Storer,

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[52] Paper No. 57
[53] Paper No. 58
[54] Paper No. 59
[55] Paper No. 60
[56] Paper No. 61
[57] Paper No. 368
[58] Paper No. 81
[59] Paper No. 82
[60] Paper No. 83
[61] Paper No. 84

the references that Clark and its expert, Dr. Wnuk, rely on in support of their argument that fluorination with DAST was unpredictable are Exhibit 2018, Krzysztof W. Pankiewicz et al., *A synthesis of 9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl) adenine and hypoxanthine. An effect of C3′-endo to C2′-endo conformational shift on the reaction course of 2′-hydroxyl group with DAST*, 57 J. ORG. CHEM. 553-59 (1992)[62] ("Pankiewicz") and Exhibit 1152, Hiroyuki Hyakawa et al., *Diethylaminosulfur trifluoride (DAST) as a fluoridating agent of pyrimidine nucleosides having a 2′,3′-vicinal diol system*, (38(5) CHEM. PHARM BULL. 1136-39 (1990) ("Hayakawa")[63]. Storer argues that Clark relies upon these references to demonstrate that using DAST in the preparation of fluoridated nucleosides may result in a "rearrangement product" and an "unfluorinated 2′-cyclo derivative." *Id.* (citing Storer Motion 1, p. 12, ll. 6-11; Ex. 2001, ¶ 156; Ex. 2145, ¶ 98). However, argues Storer, both Pankiewicz and Hayakawa teach that DAST deoxyfluorination of a nucleoside with a 2′-OH (up) proceeded with inversion to form a nucleoside with a 2′-F (down) in over 80% yields without any alleged rearrangement or unfluorinated products reported. *Id.* (citing Ex. 1152, p. 1139; Ex. 2018, p. 559; Ex. 2139, p. 149-150, ll. 10-11. Ex. 1248, p. 87, ll. 2-11).

Storer also disputes that Exhibit 2015 teaches that fluorination with DAST may proceed with double inversion resulting in a "product with unexpected stereochemistry" as Clark and its expert suggest. Storer Opp. 1, Paper 402 at 8 (citing Clark Motion 1, p 12, ll. 6-11; Ex. 2001, ¶ 156). Exhibit 2015 is Lak S.

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[62] Paper No. 61
[63] Paper No. 301

Jeong et al., *Unanticipated retention of configuration in the DAST fluorination of Deoxy-4′-thiopyrimidine nucleosides with "up" hydroxyl groups*, 35(41) TETRAHEDRON LETTERS, 7569-72 (1994) ("Jeong"). According to Storer, the title of the article explains that the double inversion was not the norm. *Id.* According to Storer, Jeong teaches that the double inversion was a result of the sulfur atom in the thiofuranose ring, which is not present in the compounds of Count 1. *Id.* (citing Ex. 2139, p. 136, ll. 8-12).

Storer also points to Exhibits 2014, 2016, and 2017, which Clark and its expert rely upon to argue that deoxyfluorination with DAST may result in an "unfluorinated dehydration product," a "rearrangement product," or an "elimination product." Storer Opp. 1, Paper 402 at 9 (citing Storer Motion 1, p. 12, ll. 6-11; Ex. 2001, ¶ 156). According to Storer, none of the DAST reactions relied upon by Clark was performed on a nucleoside. *Id.* Nevertheless, argues Storer, Exhibit 2014 teaches that "diethylaminosulfur trifluoride (DAST) appears to be the most convenient and powerful reagent for deoxyfluorination," and Exhibit 2016 teaches that "Deoxo-Fluor …and DAST … are widely used in one-step reactions for the introduction of fluorine into organic compounds." *Id.* (quoting Ex. 2014, p. 259; Ex. 2016, p. 2561). Moreover, argues Storer, Dr. Wnuk agreed that the latter statement describes the state of the art for fluorination in 2002. *Id.* (citing Ex. 2139, p. 139, ll. 13-21).

Having reviewed the parties' arguments, and the proffered evidence, we find that the art, with respect to fluoridation of tertiary alcohols, was highly unpredictable, as evidenced by Idenix's repeatedly unsuccessful attempts to

synthesize its high-priority target nucleoside, and as further evinced by the statements of Dr. Coe and Dr. Storer. *See* Ex. 2038, p. 1; Ex. 2044, p. 1.

In summary, having reviewed the *Wands* factors argued by the parties,[64] we find that (1) synthesis of a 2′-fluoro-2′-methyl nucleoside with the fluoro moiety in the "down" position required at least two years of a high-priority experimentation by persons skilled in the art, including multiple consultations with experts at the top of their fields and additional formal training; (2) the S1 application provides little in the way of direction or guidance as to how to synthesize such a compound; (3) the S1 application provides no explicit example of a 2′-fluoro-2′-methyl nucleoside, nor was an example provided by the relevant art as of the S1 application's filing date; (4) the invention is characterized as the administration of a genus of nucleosides used in the treatment of viruses, particularly those of the family *Flaviviridae* (which includes HBV and HCV) and an embodiment of the count requires a 2′-fluoro ("down") 2′-methyl nucleoside; (5) although organic fluoridation techniques were well-known in the art at the time the S1 application was filed, fluoridation of tertiary alcohols to produce a 2′ "down" tertiary fluorine was not taught or suggested by the prior art; (6) the level of skill in the art was highly sophisticated: a person possessing the ordinary level of skill in this art, as of the time of invention, would hold a doctoral degree in the field of organic, synthetic, or medicinal chemistry with at least a year's experience in the field of nucleoside synthesis or relevant drug discovery; and (7) the art, at least with respect to fluoridation of tertiary alcohols to produce a tertiary fluorine in the 2′

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[64] Neither party argued the eighth *Wands* factor, the breadth of the claims.

"down" position, was highly unpredictable. We therefore find that *Wands* factors 1, 2, 3, 5, and 7 strongly indicate that a person skilled in the art would not arrive at the claimed invention without undue experimentation. We therefore conclude that the S1 application does not enable any species of Count 1, all of which require a fluorine atom in the 2′ "down" position.

A party is accorded benefit of the date of an earlier application if its earlier application constitutes a constructive reduction to practice of the count. Bd.R. 41.201. Clark, as the party challenging Storer's accorded benefit of the S1 application, must therefore demonstrate that the S1 application does not provide a constructive reduction to practice of Count 1. SO ¶ 208.4.2. Constructive reduction to practice means a described and enabled anticipation under 35 U.S.C. 102(g)(1) in a patent application of the subject matter of Count 1. Bd.R. 41.201. Thus, even if the S1 application does not describe and enable the full scope of Count 1, Storer cannot be deprived of the filing date of the S1 application if the S1 application describes a single embodiment or species that meets all of Count 1's limitations.

Neither party disputes that all of the species of the genus contemplated within the scope of Count 1 require a fluorine atom in the "down" position and a $C(H/F)_3$ moiety in the "up" position at the 2′ carbon of the sugar ring. We have found that the analysis of the factors set forth in *Wands* compel the conclusion that, at the time the S1 application was filed, a person skilled in the art would not have been able to synthesize any of the 2′-fluoro ("down") nucleosides of Count 1 without undue experimentation. We therefore conclude that the S1 application

does not enable a single species of Count 1 and, consequently, the S1 application is not a constructive reduction to practice of Count 1. Because we find this issue to be dispositive of the motion, we do not reach Clark's other arguments. Clark Substantive Motion 1 to deny Storer the accorded benefit of its S1 application is granted.

B. Clark Substantive Motions 2 and 3

Clark Substantive Motion 2 seeks to deprive Storer of the benefit accorded with respect to Count 1 of its U.S. Appl. No. 60/466,194 (the "S2 application") filed April 28, 2003. Clark Subs. Motion 2, Paper 390 at 1. Clark Substantive Motion 3 seeks to deprive Storer of the benefit accorded with respect to Count 1 of its US Appl. No. 60/470,949 (the "S3 application") filed May 14, 2003. Clark Subs. Motion 3, Paper 391 at 1.

Clark argues that although Storer was accorded benefit of the S2 and S3 applications when the present interference was declared, Storer has not relied upon either in any of its motions in the present interference. Clark Subs. Motion 2, Paper 390 at 9; Clark Substantive Motion 3, Paper 391 at 9. According to Clark, that constitutes an admission by Storer that the S2 and S3 applications are unrelated to the subject matter in dispute between the parties. Clark Subs. Motion 2, Paper 390 at 9; Clark Substantive Motion 3, Paper 391 at 9.

Clark argues that Count 1 of the interference pertains to a method for treating HCV infection. Clark Subs. Motion 2, Paper 390 at 10; Clark Subs.

Motion 3 Paper 391 at 10 (citing Declaration,[65] p. 3, ll. 16-17; Ex. 2001, ¶¶ 45-50; Ex 2003, ¶¶ 26, 28, 29, 31-33; 40-42; Ex. 2012,[66] p. 2:8-17; Ex. 2098, col. 2221, ll. 9-52). However, argues Clark, the S2 and S3 applications are deficient because it fails to mention HCV or methods for treating HCV infection, as required by Count 1. *Id.* (citing Ex. 2001, ¶¶ 256-261; Ex. 2003, ¶¶ 140-141, 145-147; Ex. 2050,[67] pp. 1-36, Figs. 1-3). According to Clark, the S2 and S3 applications disclose processes for chemically synthesizing certain prodrugs of antiviral nucleosides. *Id.* (citing Ex. 2001, ¶¶ 58, 59; Ex. 2003, ¶¶ 49, 136-137; Ex. 2050, pp. 1, ll. 3-6, 6-9, ll. 24-9).

Clark also argues that Count 1 requires certain compounds, specifically, certain 2′-fluoro-2′-C(H/F)$_3$ nucleosides, which the S2 and S3 applications fail to disclose. Clark Subs. Motion 2, Paper 390 at 10; Clark Subs. Motion 3, Paper 391 at 10 (citing Ex. 2001, ¶ 256-261; Ex. 2050, pp. 1-36, Fig. 1-3). Therefore, argues Clark, as of the filing dates of the S2 and S3 applications, an artisan would not have believed that S2 and S3's applicants were in possession of any compound(s) falling within either of Count 1's chemical formulae, or any method(s) for treating HCV infection involving such compound(s). Clark Subs. Motion 2, Paper 390 at 11; Clark Subs. Motion 3, Paper 391 at 13 (citing Ex. 2001, ¶¶ 256-261).

Clark also argues that the S2 and S3 applications fail to provide an enabling anticipation of Count 1 because it does not teach an artisan as how to make any

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[65] Paper No. 1
[66] Paper No. 55
[67] Paper No. 112

nucleoside falling within the scope of Count 1, or teach how to treat HCV infection using any such nucleoside, without undue experimentation. Clark Subs. Motion 2, Paper 390 at 11; Clark Subs. Motion 3, Paper 391 at 13 (citing Ex. 2001, ¶¶ 256-261; Ex. 2003, ¶¶ 136-147; Ex. 2050, pp. 1-36, Fig. 1-3).

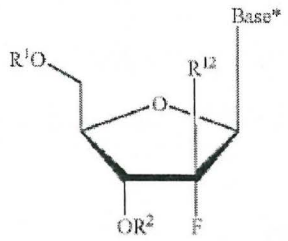
Storer argues only that Clark has failed to establish that it is entitled to the relief requested. Storer Opp. 2, Paper 403 at 2; Storer Opp. 3, Paper 403 at 2 Storer does not provide substantive argument and does not direct us to evidence to contradict Clark's arguments.

We have reviewed the disclosures of the S2 and S3 applications. For the reasons stated with respect of the S1 application, we agree with Clark that the S2 and S3 applications do not describe either the genus of Count 1 or an embodiment that meets all the limitations of that count. Clark Substantive Motions 2 and 3 to deprive Storer of the benefit accorded with respect to Count 1 of its S2 and S3 applications are granted.

C. Clark Substantive Motion 7

Clark's Substantive Motion 7 seeks judgment against Storer on the grounds that involved claims 1-12, 17, 18, 20, 33, 34, 36, 38, 49-57, 62, 64, and 76-85 of Storer's involved US Patent No. 7,608,600 B2 (the "'600 Patent") are unpatentable under 35 U.S.C. § 112, 1st paragraph for lack of enablement and written description. Clark Subs. Motion 7, Paper 154 at 1. To prevail, Clark must demonstrate that the Specification of the '600 patent does not support the full scope of the claimed subject matter.

Claim 1 of the '600 patent has been recited *supra* as part of Count 1 and we do not repeat it here. As we have related, Cark argues that the salient limitation of Storer claim 1, for purposes of enablement, is the fluorine atom in the 2′ "down" position, thus:



Ex. 1001-2, col. 2221, ll. 14-24. Storer's involved dependent claims 2-12, 17, 18, 20, 33, 34, 36, 38, and 49 all depend from claim 1 and all claim a fluorine atom in the 2′ "down" position. Ex. 1001-2. Storer's involved claims 51-57, 62, 64, and 76-85 all depend from independent claim 50, which also claims a fluorine atom in the 2′ "down" position, as do all of the involved claims depending from it. *Id.*

Storer's '600 patent issued from Storer's S4 application, which claims priority benefit of the S1 application. *See* Ex. 1001, p. 1. Clark argues that, as of June 27, 2003, the filing date of the S4 application, there was no available prior art reporting synthesis of a 2′-fluoro-2′-C(H/F)$_3$. Clark Motion 7, paper 154, at 9, citing Wnuk Decl., Ex. 2001, ¶¶ 136, 137. Clark argues further that the prior art as of 27 June 2003 would not have taught an ordinarily skilled artisan how to make the recited nucleoside without undue experimentation. *Id.* at 10.

Storer does not argue or direct us to evidence of art available prior to the June 27, 2003 filing of the S4 application that reporting or describing synthesis of

the recited nucleosides. Accordingly, because we have found *supra* that the S1 application does not enable a nucleoside as recited in Count 1, we find that the specification of the '600 patent does not enable Storer's involved claims. We therefore conclude that the involved claims 1-12, 17, 18, 20, 33, 34, 36, 38, 49-57, 62, 64, and 76-85 of '600 patent are unpatentable under 35 U.S.C. § 112, 1st paragraph, for lack of enablement.[68] Clark Substantive Motion 7 for judgment against the involved claims of Storer's '600 patent is granted.

D. Clark Substantive Motion 10

Clark next moves to deprive Storer of the benefit accorded with respect to Count 1 of US Appl. No. 10/608,907, filed June 27, 2003 (the "S4" application). Motion at 1. Clark contends that the S4 application ~~S4~~ lacks enablement, written description, and utility for subject matter anticipating Count 1. Clark Subs. Motion 10, Paper 392 at 1. Storer has opposed. Storer Opp. 10, Paper 405. Clark has replied. Clark Reply 10, Paper 422.

Because we have determined *supra* that Storer's involved claims -12, 17, 18, 20, 33, 34, 36, 38, 49-57, 62, 64, and 76-85 are unpatentable under 35 U.S.C. § 112, first paragraph, for lack of enablement, we need not reach this motion.

[68] We note that all of the remaining claims of the '600 patent similarly recite a fluorine atom in the 2′ "down" position and may likewise be unpatentable under 35 U.S.C. § 112, first paragraph, for the same reasons. Storer may wish to seek re-examination of these claims.

E. Clark Substantive Motion 5

Clark next moves to substitute its proposed count 2 or, alternatively, its proposed count 3, for Count 1. Clark Subs. Motion 5, Paper 192 at 1. Clark's Proposed Count 2 is simply its Count 164 of its '218 application. *Id.*

However, because we have already determined that Storer's involved claims are unpatentable, we *sua sponte* remove Storer's unpatentable claim 1 from the count and reformulate Count 1 as Clark's claim 164.

We therefore need not reach Clark's Substantive Motion 5.

F. Clark's Substantive Motion 8

Clark's Substantive Motion 8 seeks judgment against Storer on the ground that all of Storer's involved claims, claims 1-12, 17, 18, 20, 33, 34, 36, 38, 49-57, 62, 64, and 76-85 of Storer's '600 patent are unpatentable under 35 U.S.C. § 101, for lack of utility and, accordingly under 35 U.S.C. § 112, 1st paragraph, for lack of enablement. Clark Subs. Motion 8, Paper 155 at 1.

Our decision on Clark's Substantive Motion 7 that Storer's involved claims are unpatentable under 35 U.S.C. § 112, 1st paragraph, for lack of enablement is dispositive of the patentability of Storer's claims. Therefore, it is unnecessary for us to reach this motion. Clark's Substantive Motion 8 is consequently dismissed.

G. Clark Substantive Motion 9

Clark Substantive Motion 9 seeks judgment against Storer on the ground that all of Storer's involved claims, claims 1-12, 17, 18, 20, 33, 34, 36, 38, 49-57, 62,

64, and 76-85 of Storer's '600 patent are unpatentable under 35 U.S.C. §§ 102(e) or 103 as being either anticipated by, or obvious over, Clark's US Appl. No. 10/828,753 (the "C2 application"), filed April 21, 2004. Clark Subs. Motion 9, Paper 156 at 1.

Our decision on Clark's Substantive Motion 7 that Storer's involved claims are unpatentable under 35 U.S.C. § 112, 1st paragraph, for lack of enablement is dispositive of the patentability of Storer's claims. Therefore, it is unnecessary for us to reach Clark Substantive Motion 9.

H. Clark Miscellaneous Motion 18

Clark has moved to exclude the following Storer Exhibits: 1132, 1175-76, 1177, 1200, 1201, 1228, 1229, 1231, 1232, and 1233. Clark Misc. Motion 18, Paper 427 at 1.

1. Storer Exhibit 1132

Clark argues that Storer Exhibit 1132, the Declaration of Masad J. Damha, Ph.D., (the "Damha Declaration") is inadmissible under SO ¶ 105.6 because it is an affidavit without an original signature. Clark Misc. Motion 18, Paper 427 at 1. According to Clark, Dr. Damha, Storer's declarant, testified at his deposition that he did not sign a paper copy of Exhibit 1132 in ink, but instead inserted a digital image of his signature. *Id.* (citing Ex. 1194 , p. 26, ll. 14-24). Furthermore, argues Clark, there is no original copy of Exhibit 1132 with a handwritten original

signature that could have been retained or made available on demand, which is also in violation of SO ¶ 105.6. *Id.* (citing Ex. 1194, pp. 26-27, ll. 25-4).

Alternatively, argues Clark, paragraphs 61-81 of the Damha Declaration should be excluded under Federal Rule of Evidence 702 because Dr. Damha's opinions expressed in these paragraphs are not based on sufficient facts or data. Clark Misc. Motion 18, Paper 427 at 2. According to Clark, when opining that it would have been trivial for an artisan to make 2′-fluoro-2′-methyl nucleosides, Dr. Damha did not take into account Storer's own documents from the prior '871 interference (e.g., Ex. 2029, Ex. 2035, Ex. 2041, Ex. 2042, and Ex. 2043).

Storer responds that Dr. Damha verified during his deposition that he personally inserted his digital signature into his Declaration. Storer Opp. 18, Paper 29 at 1 (citing Ex. 1194, p. 26, ll. 19-24. Therefore, argues Storer, although Dr. Damha did not handwrite his signature on a paper copy of his declaration, he did verify that he personally electronically signed the declaration. *Id.* Storer submits that the Board should accept this as sufficient. *Id.*

Storer also argues that Clark did not timely object to Exhibit 1132 at the deposition and also failed to request a conference call with the Administrative Patent Judge managing the interference to seek authorization to belatedly object to Exhibit 1132. Storer Opp. 18, Paper 29 at 1 (citing 37 C.F.R. § 41.155(a)).

Dr. Damha has affirmed that the digital signature is a reproduction of his own signature and that the declaration was his own. We therefore decline to exclude the Exhibit on this ground.

More substantially, we agree with Storer that whether Dr. Damha examined the '871 interference documents prior to forming his opinion on whether a person of ordinary skill could have synthesized 2′-fluoro-2′-methyl nucleoside compounds is a question of the probative weight of the opinion testimony and not one of admissibility. We held, *supra*, that Dr. Damha was qualified as an expert. He may express his opinions on matters relevant to this interference. Federal Rule of Evidence 702 states that a "witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if … the testimony is based on sufficient facts or data." Fed. R. Evid. 702(b).

We therefore decline to exclude Exhibit 1132.

2. Storer Exhibits 1175 and 1176

Clark next argues that Storer Exhibits 1175[69] and 1176[70], which comprise two emails to the Patent Trial and Appeal Board concerning the '871 interference, with copies to Administrative Patent Judge New, discuss Storer's allegations of inequitable conduct and request authorization to move for additional discovery in the present interference, are inadmissible in their entirety because they are irrelevant under Rule 402, as well as confusing and a waste of time under Rule 403. Clark Misc. Motion 18, Paper 427 at 3.

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[69] Paper No. 458
[70] Paper No. 459

Storer was not authorized to file a motion asserting inequitable conduct and has not raised the issue in any of its substantive or contingent motions considered herein. Because this evidence is unrelated to any of the matters before us we decline to address the admissibility of Exhibits 1175 and 1176 as an evidentiary matter. However, because the exhibits are extraneous to this proceeding we order that they be expunged from the record. Bd.R. 7(a) & 122(c)(1)(iii).

3. Storer Exhibit 1177

Storer Exhibit 1177[71] is a copy of an order (Docket No. T-1156-12) from Federal Court of Canada, regarding the litigation with respect to the Canadian versions of Storer's involved patent and Clark's involved application in that venue. Clark seeks exclusion of Exhibit 1177 on substantially the same grounds that it seeks exclusion of Exhibits 1175 and 1176. Clark Misc. Motion 18, Paper 427 at 4.

Storer has not raised, in any of its substantive or contingent motions, any argument that relies upon this Exhibit and, having reviewed the Exhibit, we can discern no purpose for it to be included in this proceeding. Because the exhibit appears to be extraneous to this proceeding, we decline to consider it as an evidentiary matter and order that it be expunged from the record of this proceeding. Bd.R. 7(a) & 122(c)(1)(iii).

[71] Paper No. 460

4. Storer Exhibit 1200

Clark next seeks exclusion of Exhibit 1200, the Second Declaration of Dr. Damha. Clark Misc. Motion 18, Paper 427 at 5. According to Clark, Dr. Damha failed to consider relevant information. Clark argues that Dr. Damha did not take into account the Storer Documents when forming his view that it would have been trivial for an artisan to make 2′-fluoro-2′-methyl nucleosides as of June 28, 2002. *Id.* (citing Ex. 1244, pp. 26-40, ll. 19-15). Clark argues further that Dr. Damha testified that such evidence was not important and that there was not "any chance" that it could have affected his opinions, despite the Board having previously found it significant. *Id.* (citing Ex. 1244, pp. 31-40, ll. 15-15).

We have related *supra*, with respect to Storer's Exhibit 1132, why the credibility of Dr. Damha's opinion testimony is a probative question on the merits of Storer's substantive motions. The issue is one of the weight of the testimony rather than one of admissibility. We employ the same reasoning here. Clark's motion to exclude Exhibit 1200 is denied.

5. Storer Exhibit 1201

Storer Exhibit 1201 is the Second Declaration of Raffaele De Francesco, Ph.D. According to Clark, Dr. De Francesco opines on an artisan's ability to perform high throughput testing of compounds for activity against hepatitis C virus ("HCV") using an HCV replicon assay during the 2000-2003 timeframe. Clark Misc. Motion 18, Paper 427 at 5 (citing Ex. 1201, ¶¶ 82, 95-101). Clark argues that Dr. De Francesco's opinions are based on unpublished techniques allegedly

used in his own labs. Because the reaction conditions and experimental processes for these screening experiments were not published, argues Clark, they were not available to the artisan to utilize, test or publicly critique. Clark Misc. Motion 18, Paper 427 at 5-6 (citing Ex. 2171, ¶ 128). Therefore, contends Clark, De Francesco's testimony regarding his non-public activities within his laboratory does not provide any insight whatsoever into any issue pending in this. Motion at 6.

Storer did not oppose Clark's motion to exclude Exhibit 1201. Nevertheless, we are not persuaded by Clark's arguments. As we have related *supra*, with respect to Storer's Exhibits 1132 and 1200, the credibility of Dr. De Francesco's opinion testimony is a probative question on the merits of Storer's motions. The issue is one of weight and not one of admissibility. We employ the same reasoning here. Clark's motion to exclude Exhibit 1201 is denied.

6. Storer Exhibit 1228 and 1229

Storer Exhibit 1228[72] is the transcript of the deposition of Stanley Moncrief Lemon and Storer Exhibit 1229[73] is the transcript of the deposition of Jeffrey Scott Glenn, both taken on Tuesday, July 31, 2012. Clark Misc. Motion 18, Paper 427 at 7. Clark argues that both transcripts are inadmissible as hearsay under Rule 802, and under SO ¶¶ 157.1 and 157.3, because they are transcripts of depositions taken in the prior 105,871 interference. *Id.* Clark contends that if Storer wanted to rely

[72] Paper No. 531
[73] Paper No. 532

on the testimonies of Drs. Lemon and Glenn, it should have submitted a new declaration from both individuals in the present case, thereby making them subject to cross-examination in this interference. *Id.*

Storer points out that Clark has failed to demonstrate that Storer relies on Exhibits 1228 and 1229 to prove the truth of any statements therein. Storer Opp. 18, Paper 429 at 7, 8. Storer points out that Clark has not directed the Board to any statements in either Exhibit that Storer relies on to prove the truth of an asserted matter. *Id.* Finally, Storer argues that that Clark was a party to the prior 105,871 interference and that Clark cross-examined both deponents during their respective depositions. *Id.* (citing Exs. 1228; 1229). Moreover, contends Storer, Clark submitted the Declarations of Drs. Lemon and Glenn, which was the basis for the deposition as Exhibit 2167. *Id.* Therefore, argues Storer, Clark is not prejudiced by the introduction of Exhibits 1228 into evidence. *Id.*

We agree that Storer has not relied upon Exhibits 1228 and 1229 in support of any of its arguments in its substantive or contingent motions. Accordingly, we can discern no purpose for it to be included in this proceeding. We decline to consider it as an evidentiary matter and order that it be expunged from the record of this proceeding. Bd.R. 7(a) & 122(c)(1)(iii).

7. Storer Exhibits 1231, 1232, and 1233

Storer Exhibit 1231 is the laboratory notebook by Jingyang Wang, an employee of Idenix Pharmaceuticals, Inc., one of the Storer real parties-in-interest.

Clark contends that Exhibit 1231 is inadmissible under Rules 402, 403, 802, and 901(a), and SO ¶¶ 152.2.2 and 157.1. Clark Misc. Motion 18, Paper 427 at 7.

We considered Exhibits 1232 and 1233 with respect to our conclusion that the S1 application did not enable the embodiments of a 2′ fluoro "down" nucleoside within the scope of Count 1. Clark prevailed upon that issue notwithstanding the consideration of these exhibits. Exclusion of the exhibits would not influence the outcome of our review. It is therefore unnecessary for us to consider the admissibility of the exhibits.

8. Summary

For the reasons set forth above, Clark's Miscellaneous Motion 18 is denied.

III. STORER MOTIONS

A. Storer Substantive Motion 5

Storer moves to substitute proposed Count B for Count 1 and to be accorded benefit of the S1 application. Motion at 1. All of the species encompassed by Storer's proposed Count B and disclosed in the Genus Disclosure of Storer's involved application have a fluorine atom in the 2′ "down" position. *See* Storer Subs. Motion 5, Paper 157 at App'x 8-2 ("R^7 is F"; "[F is shown in the 2' "down" position of the above formula]"). We have related *supra* that the claims of Storer's involved application fail to provide an enabling disclosure for any of the embodiments of the nucleosides within the scope of its involved claims. All of

those claims are characterized by a fluorine in the 2′ "down" position. As a result of our determination we removed Storer's claim 1 as an alternative of the count. Storer's proposed Count B broadens the species substituents at other positions of the nucleotide but includes the fluorine in the 2′ "down" position. Thus, Storer's proposed Count B is unsuitable as a vehicle for determining priority in this interference for the same reasons that Storer's Claim 1 was unsuitable. We therefore deny Storer's Substantive Motion 5.

B. Storer Substantive Motion 11

Storer next argues that Clark's involved claims are unpatentable under 35 U.S.C. § 102(e)(2) and/or 35 U.S.C. §§ 102(e)(2)/103(a) over Storer's '600 patent. Storer Subs. Motion 11, Paper 158 at 1. Storer does not challenge that the Clark '218 application has an effective filing date of May 30, 2003, the date Clark's '368 provisional application was filed. *Id.*

Storer argues that its '600 patent, which it cites as prior art under 35 U.S.C. § 102(e), has an effective filing date of June 28, 2002, the filing date of its S1 application, which precedes the May 30, 2003, filing date of Clark's '368 application. Storer Subs. Motion 5, Paper 157 at 2. Therefore, argues Storer, the '600 patent is prior art to the Clark claims. *Id.*

We have related *supra* why ~~we~~ Storer's involved claims are not supported by an enabling disclosure of an embodiment having a 2′-fluoro "down" nucleoside. For the same reason, the earlier S1 application fails to provide an enabling disclosure for nucleoside with the fluorine in the down position. Storer is not

entitled to the benefit of the June 28, 2002, filing date of the S1 application. Storer's '600 patent is not prior art for Clark's '638 application. We therefore deny Storer's Substantive Motion 11.

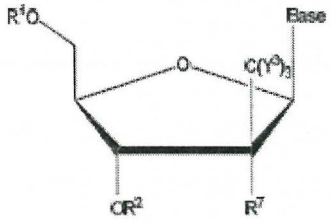
C. Storer Contingent Responsive Motion 14

Storer Contingent Responsive Motion 14 seeks to add a new claim, claim 14 to the interference if any of Clark Substantive Motions 7, 8, or 9 are granted. Storer Cont. Motion 14, Paper No. 327 at 1.

Because we have granted Clark Substantive Motion 8, we now address Storer Contingent Motion 14.

Storer Claim 14 recites:

> 14. A method for the treatment of a host infected with a hepatitis C virus, comprising administering to the host infected with a hepatitis C virus an effective amount of a compound of the formula:



> or a pharmaceutically acceptable salt thereof, wherein:
>
> Base is selected from the group consisting of thymine, cytosine, 5-fluorocytosine, 5-methylcytosine, 6-azapyrimidine, 6-azacytosine, 2- and/or 4 mercaptopyrimidine, uracil, 5-halouracil, 5-fluorouracil, C^5-alkylpyrimidine, C^5-benzylpyrimidine, C^5-halopyrimidine, C5-vinylpyrimidine, C^5-acetylenic pyrimidine, C^5-acyl pyrimidine, C^5-

> amidopyrimidine, C^5-cyanopyrimidine, C^5-iodopyrimidine, C^6-iodo-pyrimidine, C^5-Br-vinyl pyrimidine, C^6-Br-vinyl pyrimidine, C^5-nitropyrimidine, C^5-aminopyrimidine, 5-azacytidinyl, 5-azauracilyl;
>
> R^7 is F;
>
> R^1 is H; phosphate; monophosphate, diphosphate; triphosphate; a stabilized phosphate prodrug; acyl; lower acyl; alkyl; lower alkyl; sulfonate ester; alkyl or arylalkyl sulfonyl; methanesulfonyl; benzylsulfonyl; a lipid; a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered in vivo provides a compound wherein R^1 is H or phosphate;
>
> R^2 is phosphate; monophosphate; diphosphate; triphosphate; a stabilized phosphate prodrug; acyl; lower acyl; alkyl; lower alkyl; sulfonate ester; alkyl or arylalkyl sulfonyl; methanesulfonyl; benzylsulfonyl; a lipid; a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered in vivo provides a compound wherein R^2 is H or phosphate; and wherein each Y^3 is H.

Motion App'x at 2-1-2. We note that all of the embodiments of Storer's proposed claim 14 possess a fluorine atom in the 2′ "down" position.

Responsive motions may be filed to cure a claim defect raised on a notice of requested relief or a substantive motion. Bd.R. 41.121(a)(2). However, we have related *supra* why the S1 application fails to enable a fluorine atom in the 2′ "down" position of any of the embodiments of the nucleoside species within the scope of count 1. Storer's proposed claim 14 fails to cure this defect of the Storer claims corresponding to Count 1. We therefore deny Storer's Contingent Responsive Motion 14.

D. Storer Contingent Miscellaneous Motion 15

Storer Contingent Motion 15 seeks the addition to this interference of Storer US Appl. No. 14/220,534, (the "'534 application") filed March 20, 2014. Storer Cont. Motion 15, Paper 328 at 1. Storer's proposed Claim 14 is the sole claim pending in the '534 application. *Id.* The '534 application claims the benefit accorded the S1 and S4 applications. *Id.* at 2.

When Storer was authorized to file the contingent responsive motion to add Storer's new claim 14, Storer was also required to file a contingent miscellaneous motion to add the new continuation application with the new claim to the interference. *See* Order Responsive Motion Bd.R. 41.121(a)(2), Paper 326, at 3:1-3. Storer Contingent Miscellaneous Motion 15 serves that purpose. Storer Cont. Motion 15, Paper 328 at 1.

Because we have denied Storer's Contingent Responsive Motion 14 to add its new claim 14, we do not reach Storer's Contingent Motion 15 to add the '534 application to the instant interference.

E. Storer Miscellaneous Motion 16

Storer seeks to exclude the following Exhibits, in full or in part: Storer Exhibits 1194, 1243, 1244, and exclusion of Clark Exhibits 2088, and 2100. Storer Misc. Motion 16, Paper 425 at 1-5.

1. Storer Exhibit 1194

Storer Exhibit 1194 is the deposition of Dr. Damha, taken on April 15, 2014. Storer argues that the questions posed by Clark's counsel at page 81, lines 9 to 19 page 85, lines 14 were beyond the scope of Dr. Damha's direct testimony given in Exhibit 1132 and/or were irrelevant as to whether one of ordinary skill in the art as of June 28, 2002 would have been able to synthesize a 2′-fluoro-2′-methyl-nucleoside at issue. Storer Misc. Motion 16, Paper 427 at 1. Specifically, Storer argues that Dr. Damha did not, in his Declaration, address Idenix's post-June 28, 2002 efforts to synthesize a 2′-fluoro-2′-methyl-nucleoside, which was the subject of the questions posed by Clark's counsel in the disputed pages. *Id.* at 1-2.

Clark responds that, first, impeachment evidence is always relevant and within the scope of permissible cross-examination. Clark Opp. 16, Paper 430 at 1 (citing Fed. R. Evid. 611(b); 702).

Second, Clark denies that, in the disputed questions in Exhibit 1194, the questions exceeded the scope of Dr. Damha's direct testimony. Clark Opp. 16, Paper 430 at 3. Clark contends that the questions went to the bases for the opinions proffered in Exhibit 1132 and, specifically, whether those opinions took into account Idenix's synthesis efforts. *Id.*

Third, Clark points out that Storer's counsel did not object to the questions posed by Clark's counsel pp. 82, ll.11-13; 82, ll. 15-18; 82, ll. 20-21; 82, l. 23; 82, l. 25; 83, ll. 3-4; 83, ll. 6-7; and 85, ll. 10-13 of Exhibit 1194, and to which Dr. Damha at pp. 82, l. 14; 82; l. 19, 82, l. 22; 82, l. 24; 83, l. 2; 83, l. 5; 83, l. 8; and

85, l. 14, respectively, responded. Clark Opp. 16, Paper 430 at 3 (citing Ex. 1194). Therefore, argues Clark, these questions and answers should not be excluded. *Id.*

We are not persuaded by Storer's arguments. In the disputed passages of Exhibit 1132, Dr. Damha is questioned repeatedly whether, in arriving at his opinion that one of ordinary skill in the art would be aware of "a method for preparing a 2′-F-2′-methyl-ribonucleoside of the '350 Application and within the scope of Claim 38 of the Storer Patent," he had been made aware of, or considered, any of Idenix's efforts to synthesize the compound during the interval between 2002 and 2005. For example, during the Dr. Damha's deposition, he responded to the questions as below:

> Q. So you're not aware that in the prior interference Idenix put forth its story about how its chemists tried to make 2′-fluoro-2′-methyl nucleosides during the 2002 to 2005 time period?
>
> MR. KINTON: Same objection. Beyond the scope.
>
> A. No.
>
> Q. So then you couldn't have considered any of Idenix's story about its attempt to make those compounds in forming your opinions?
>
> A. None whatsoever.
>
> Q. And did you consider any Idenix documents about trying to make 2′-fluoro-2′-methyl nucleosides when you formed your opinion?
>
> A. No.
>
> Q. Did you consider any Idenix lab notebooks when forming your opinion?

A. On how to make these compounds, no.

Q. What about Idenix's meeting minutes?

A. No.

…

Q. Did you ever ask to see such information when forming your opinions?

A. No.

Q. Why not?

MR. KINTON: Objection. Irrelevant.

Ex. 1194, p. 82, ll. 3-24; p. 83, ll. 6-10. These, and the other disputed passages, all inquire whether Dr. Damha had reviewed, or had knowledge of, any documents concerning Idenix's research efforts between 2002 and 2005. Dr. Damha responded in the negative to this entire line of questioning:

Q. Do you think what Idenix actually tried in terms of attempting to make a 2′-fluoro-2′-methyl nucleoside might be important when forming your opinion?

MR. KINTON: Objection. Irrelevant. Assumes facts.

A. No, not at all. I formed my opinion on literature and knowledge that I have gained as a nucleoside nucleic acid chemist. And in fact, having used procedures that are directly applied to the synthesis of the 2′-methyl-2'-fluoro compounds.

Ex. 1194, pp. 84-85, ll. 22-9. Thus, this line of questioning by Clark inquires as to the materials that formed the basis for Dr. Damha's opinion expressed in his Declaration. As such, it is neither beyond the scope of Dr. Damha's declaration, nor is it irrelevant. Moreover, Clark is entitled to attempt to impeach the credibility of Storer's expert on cross-examination. FRE 611(b). Storer's motion to exclude the cited passages of Storer's Exhibit 1194 is consequently denied.

2. Storer Exhibit 1243

Storer Exhibit 1243[74] is the transcript of the deposition of Dr. De Francesco. Storer moves to exclude certain passages in the Exhibit, *viz.*, page 81, lines 12-13 and 21-22 and page 82, lines 6-8 as exceeding the scope of Dr. De Francesco's direct testimony in his Declaration (Ex 1201). Storer Misc. Motion 16, Paper 427 at 3. According to Storer, Dr. De Francesco did not address in his declaration the disclosure in Exhibit 1003 of the bases for particular compounds, including Formula (IV), which was the subject of the questions posed by Clark's counsel.

Clark responds that, first, Dr. De Francesco's testimony in the contested passages is admissible because Clark's counsel's questions were within the scope of Dr. De Francesco's direct testimony in his Declaration or, alternatively, went to a matter affecting Dr. De Francesco's credibility. Clark Opp. 16, Paper 430 at 4 (citing FRE 611(b), 702).

We are not persuaded by Storer's arguments. In his Declaration, Dr. De Francesco opined:

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[74] Paper No. 544

> The '350 and '907 applications state that the compounds of the invention exhibit antiviral activity against *Flaviviridae* viruses such as HCV, and can be used to treat infections by those viruses. Ex 1003, at 44:3-4, 57:15-19; Ex 1002, at 46:3-4, 58:4-9. As of June 28, 2002 and June 27, 2003, persons skilled in the art would have believed that the Relevant Compounds could have anti-HCV activity because: (i) the Relevant Compounds are nucleoside analogs, and it was known at the time that certain nucleoside analogs exhibit antiviral activity due to interference with viral polymerases required for replication of viral genetic material (referred to herein as "genome replication"), as described in ¶¶39-40;
>
> (ii) it had been shown experimentally at the time that certain 2′-modified nucleosides exhibit anti-*Flaviviridae* activity, in particular against BVDV and YFV, as described in ¶¶41-46;
>
> (iii) persons skilled in the art would have believed that nucleoside analogs that exhibit activity against BVDV are likely to also exhibit activity against HCV, and that nucleoside analogs that exhibit activity against BVDV and YFV are highly likely to also exhibit activity against HCV, as described in ¶¶47-67;
>
> (iv) as of June 27, 2003, it had been experimentally shown that certain 2′- modified nucleosides exhibit anti-HCV activity, as described in ¶¶68-70; and
>
> (v) there were no specific reasons to doubt anti-HCV activity of the Relevant Compounds, as described in ¶71.

Ex. 1201, ¶ 21. In the contested passages of Exhibit 1243, Dr. De Francesco states:

> Q. Would you turn back to page 57 of the '350 application, which is Exhibit 1003?
> …

A. Uh-huh.

Q. And could you identify for me what the base is for that formula?

MR. FRIEBEL: Objection, beyond the scope of his declaration.

...

A. (Perusing.) No. Sorry. This is — I think this is beyond my — it would require a better understanding of chemistry than I have.

Q. So you have no idea what the base would be?

MR. FRIEBEL: Same objection.

A. (Perusing.) I didn't review these as part of my opinion because I don't think this was requested to me. Tentatively, I would say it's one of the group — must be one of the group of bases described in the previous pages, I guess.

Q. So we were talking about the compounds at pages 1551 previously. Would that be previous pages?

MR. FRIEBEL: Same objection, beyond the scope of his original — of his second declaration.

A. (Perusing.) Yeah, I believe herein means one of the bases described in pages 48, 49 to 54, but I'm not sure. I mean, again, I'm not a chemist, so I don't — it's a tentative answer.

Ex. 1243, pp. 81-82, ll. 7-16.

Determining the scope of cross-examination is within the sound discretion of the administrative tribunal. *See, e.g., Guise v. Dep't of Justice*, 330 F.3d 1376, 1379 (Fed. Cir. 2003). Dr. De Francesco has explicitly declared that he has studied Storer Exhibit 1003, the '350 application, as part of the preparation for giving his

expert opinion. Ex. 1243, ¶ 10. Because Dr. De Francesco places no limiting language on this statement in his Declaration, we assume that he has reviewed the entire document and that questions concerning the contents of the document on cross-examination are not beyond the scope of his Declaration. Therefore, the contents of the '350 application are within the scope of his Declaration. The line of questioning in the disputed passages goes to the basis for the formation of that opinion, although his statements ("it would require a better understanding of chemistry than I have") may undermine his credibility as an expert witness with respect to the chemistry of nucleoside bases. Nevertheless, the credibility of a witness' opinion, and the probative weight we consequently ascribe to that testimony, is a substantive issue and not one of admissibility. We consequently deny Storer's motion to exclude the contested passages of Exhibit 1243.

3. Storer Exhibit 1244

Storer Exhibit 1244[75] is the Second Deposition of Dr. Damha, taken on June 20, 2014. Storer moves to exclude certain passages in the Exhibit, *viz.*, page 26, line 19 to page 29, line 25; page 33, line 11 to page 36, line 2; and page 36, line18 to page 40, line 15 as exceeding the scope of Dr. Damha's direct testimony in his Declaration (Ex. 1200). Storer Misc. Motion 16, Paper 427 at 4. Specifically, Clark contends that Dr. Damha did not address, in his Declaration, Idenix's post-June 28, 2002 effort in synthesizing a 2′-fluoro-2′-methyl nucleoside, the subject of the questions posed by Clark's counsel in the contested passages. *Id.*

[75] Paper No. 545

In response, Clark repeats the argument that it made with respect to Ex. 1195 *supra*: that the testimony that Storer seeks to exclude is relevant to determining whether Dr. Damha's direct testimony in Exhibit 1200 should be given any weight, and whether it is relevant to assessing Dr. Damha's credibility, particularly with regard to Dr. Damha's opinions about whether an artisan could have made 2′-fluoro-2′-methyl nucleosides without undue experimentation. Clark Opp. 16, Paper 430 at 5. Clark also contends that Dr. Damha's alleged failure to consider Idenix's extended efforts to synthesize the compounds affects his credibility as an expert witness. *Id.*

We agree with Clark. As we related *supra*, the lines of questioning objected to by Storer inquire as to the materials that formed the basis for Dr. Damha's opinion, as expressed in his Declaration and the extent of Dr. Damha's knowledge of Idenix's efforts at synthesis of 2′-fluoro-2′-methyl nucleosides. Moreover, Clark is entitled to attempt to impeach the credibility of Storer's expert in cross-examination. FRE 611(b). As such, it is neither beyond the scope of Dr. Damha's declaration, nor is it irrelevant. Storer's motion to exclude the cited passages of Storer's Exhibit 1194 is denied.

4. Clark Exhibit 2088

Clark Exhibit 2088[76] is the Declaration and curriculum vitae of Dr. Jean-Pierre Sommadossi, one of the inventors of Storer's '600 patent. Storer Misc. Motion 16, Paper 427 at 5. Storer argues that although Exhibit 2088 refers to

[76] Paper No. 568

Exhibit 1 (a copy of Tables 4 and 5 from Chapter Two of B.N. Fields et al., *Fields Virology*, Lippincott-Raven, Philadelphia (3rd ed. 1996)) at 3, ¶ 11.), Exhibit 2088 does not in fact contain an Exhibit 1. *Id.* Therefore, argues Storer, Exhibit 2088 is incomplete and should be excluded under Federal Rule of Evidence 106. *Id.*

Storer also argues that Clark relies on Exhibit 2088, and particularly ¶ 15, to prove that one cannot predict a compound's activity against another virus without testing it. Storer Misc. Motion 16, Paper 427 at 5 (citing Clark Substantive Motion 8[77], at 11, ll. 13-14). Consequently, argues Storer, Clark Exhibit 2088 is an out-of-court statement made by a declarant who has not testified in this proceeding and the statement is offered to prove its truth. *Id.* Therefore, Storer contends, Exhibit 2088 is also inadmissible as impermissible hearsay. *Id.* (citing FRE 802).

As an initial matter, Federal Rule 106 is not an exclusionary rRule. Federal Rule 106 states: "If a party introduces all or part of a writing or recorded statement, an adverse party may require the introduction, at that time, of any other part--or any other writing or recorded statement--that in fairness ought to be considered at the same time." Fed. R. Evid. 106. Storer has not requested completion of the record, and we therefore consider any such request waived.

5. Clark Exhibit 2100

Clark Exhibit 2100[78] is a document of the European Patent Office ("EPO"), purportedly reporting of a consultation by the EPO with applicant/representative

[77] Paper No. 155
[78] Paper No. 576

Idenix Pharmaceuticals, Inc., the real party-in-interest in the instant interference, with respect to EPO Application No. 03 761 744.6.

Storer argues that Clark relies on Exhibit 2100 to prove that Exhibit 1002's[79] Formula (IX) does not provide for R^1 to be di- or triphosphate and thus does not describe certain Storer claims. Storer Misc. Motion 16, Paper 427 at 5-6. As such, contends Storer, Exhibit 2100 constitutes impermissible hearsay and should be excluded. *Id.* at 6.

We do not see the relationship of Exhibit 2100 to the dispositive issue with respect to Storer's involved claims, *viz.*, the enablement of a 2′-fluoro "down" -nucleoside. Accordingly, we can discern no purpose for it to be included in this proceeding. We decline to consider it as an evidentiary matter and order that it be expunged from the record. Bd.R. 7(a) & 122(c)(1)(iii).

6. Summary

For the reasons set forth above, Storer's Miscellaneous Motion 16 is denied.

IV. CONCLUSION

For the reasons set forth above:

1. Clark Substantive Motion 1 to deprive Storer of the benefit of its US Appl. No. 60/392,350 is GRANTED.

[79] Papers Nos. 319-322

2. Clark Substantive Motion 2 to deprive Storer of the benefit accorded with respect to Count 1 of its U.S. Appl. No. 60/466,194 is GRANTED.

3. Clark Substantive Motion 3 to deprive Storer of the benefit accorded with respect to Count 1 of its U.S. Appl. No. 60/470,949 is GRANTED.

4. Clark Substantive Motion 10 to deprive Storer of the benefit accorded with respect to Count 1 of US Appl. No. 10/608,907 is DISMISSED.

5. Clark Substantive Motion 7 for judgment against Storer's US Patent No. 7,608,600 B2 on the grounds of unpatentability under 35 U.S.C. § 112, 1st paragraph for lack of enablement and written description is GRANTED.

6. Clark Substantive Motion 5 to substitute its proposed alternate count 2 for the present Count 1 of the interference is DISMISSED.

7. Clark Substantive Motion 8 for judgment against Storer's US Patent No. 7,608,600 B2 on the ground of unpatentability under 35 U.S.C. § 101, for lack of utility, and accordingly under 35 U.S.C. § 112, 1st paragraph, for lack of enablement is DISMISSED.

8. Clark Substantive Motion 9 for judgment against Storer's US Patent No. 7,608,600 B2 on the ground of unpatentability under 35 U.S.C. §§ 102(e) or 103 as being either anticipated by, or obvious over, Clark's US Appl. No. 10/828,753 is DISMISSED.

9. Clark Miscellaneous Motion 18 to exclude evidence is DENIED. We *sua sponte* order that Storer Exhibits 1175, 1176, 1177, 1228, and 1229 be expunged.

10. Storer Substantive Motion 5 to substitute proposed count B for Count 1 is DENIED.

11. Storer Substantive Motion 11 for judgment against Clark on the grounds of unpatentability of all of Clark's involved claims as anticipated under 35 U.S.C. § 102(e) and/or 103 is DENIED.

12. Storer Contingent Motion 14 to add a new claim is DENIED.

13. Storer Contingent Motion 15 to add an application to the interference is DISMISSED.

14. Storer Miscellaneous Motion 16 to exclude evidence is DENIED. We *sua sponte* order that Clark Exhibit 2100 be expunged.

15. Party Clark shall be designated Senior Party for any further proceedings according to the Redeclaration issued herewith.

IT IS SO ORDERED

cc:

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