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Cubist v. Hospira: Certificate of Correction instead of Reissue?

Rick Gallagher – firm lunch – December 16, 2015

Cubist v. Hospira

A patent issued with claims that referred to a chemical compound by a depiction of a structural formula for the compound. The patentee later discovered that the structural formula was erroneous (and in fact showed a different chemical compound).

The patentee used Certificate of Correction procedure to correct the error, rather than correcting the error by filing a reissue application. Even though this involved significant change and depended upon post-filing scientific evidence, it was held to be OK.

Cubist v. Hospira

Cubist Pharmaceuticals, Inc.

versus

Hospira, Inc.

805 F.3d 1112

U.S. Court of Appeals, Federal Circuit

November 12, 2015

Cubist v. Hospira

- This is a decision of an appeal from the U.S. district court for the district of Delaware.
- The appeal was decided by a 3-judge panel: Evan J. Wallach, William C. Bryson, and Todd M. Hughes.
- The decision was written by Judge Bryson. There was no dissent (nor was there any separate concurring opinion).

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This case arises under the Drug Price Competition and Patent Term Restoration Act of 1984, a.k.a. the Hatch-Waxman Act. The Hatch-Waxman Act provides a course of action for the public to iron out patent rights in medicines which have been approved for sale in this country by the FDA. The interested party, usually a generic drug manufacturer, does not have to produce and market a product and wait to be sued by the patent owner. Instead, the generic drug manufacturer can file an application in the FDA for approval to market the product, and the patent owner can sue for infringement based upon the application. No actual infringement is necessary.

In this case, Hospira filed a request with the FDA to sell a generic version of the antibiotic daptomycin, which is covered by a patent owned by Cubist. In accordance with the Hatch-Waxman Act, Cubist sued Hospira for patent infringement.

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Daptomycin is used to treat drug-resistant bacteria. It was originally discovered by Eli Lilly & Co.

Lilly stopped development of daptomycin when it appeared that daptomycin had dangerous side effects. Cubist bought the rights to it, and figured out how to fix the problem. Under the brand name Cubicin, daptomycin currently generates a billion dollars in sales annually.

The original patent on daptomycin expired in 2002. This case involved five follow-on Cubist patents. Four are directed to developments relating to purity and dosage. Those four were held by the district court to be invalid for obviousness over earlier publications relating to daptomycin. A portion of the decision in *Cubist v. Hospira* deals with Cubist's appeal of that invalidity holding. The obviousness issue is not discussed in this presentation.

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As for the fifth Cubist patent, the district court held the two asserted claims therein not invalid and ruled that Hospira's proposed products infringed those claims (claims 18 and 26). This presentation deals with the Federal Circuit's treatment of Hospira's appeal against this ruling by the district court.

The patent of interest is RE39,071, with a reissue date in 2006. The original patent (the '226 patent) was issued in June of 1999, on an application filed in 1991 (that is, before June 8, 1995). The '226 patent had a term that ran 17 years from its issue date, so the '071 patent will expire in June of 2016.

Hospira's appeal argued that the claims are not valid. The Hospira appeal focused on a Certificate of Correction which was granted to Cubist with regard to the '071 patent. The Certificate corrected a diagram of the chemical structure of a compound described in the specification and recited in claims 18 and 26 of the patent.

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The asserted claims in the ‘071 patent are drawn to compositions comprising a combination of three compounds, having structural formulas 1, 2, and 3. The third compound (Formula 3) is daptomycin.

The specification of the ‘071 patent describes the Formula 3 compound in three ways:

(1) It refers to the compound as “an A-21978C cyclic peptide.” According to the specification, A-21978C cyclic peptides “are prepared from the A-21978C antibiotics,” which are “a group of closely related, acidic peptide antibiotics” that are described in an earlier U.S. patent.

(2) The specification of the ‘071 patent also refers to the Formula 3 compound by the code name LY46032, which was a Lilly code name known in the art to refer to daptomycin.

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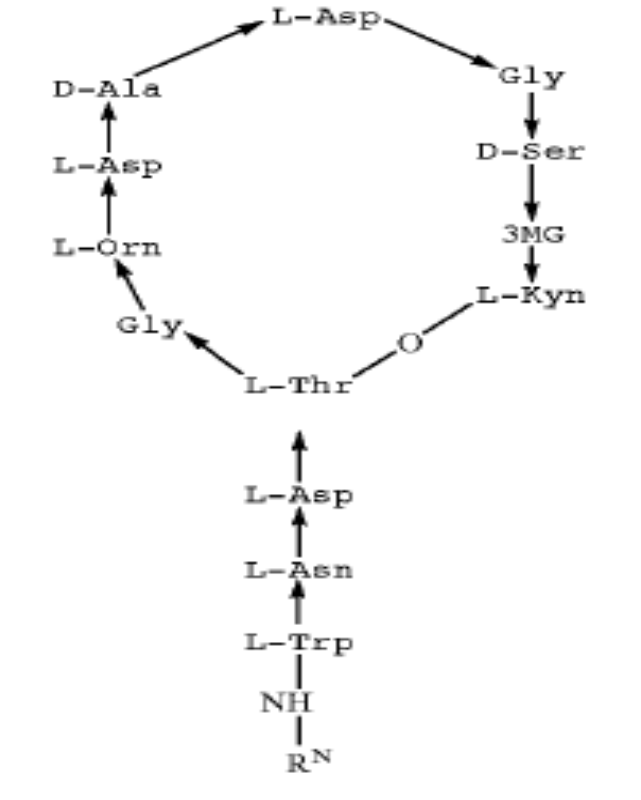
(3) The specification also states that the Formula (3) compound has the structure:



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In that formula, the 3-letter designations, such as Asp, Asn, and Trp refer to amino acids, which make up portions of the daptomycin molecule. Asp, Asn, and Trp are, respectively, aspartic acid, asparagine, and tryptophan.

Amino acids can exist in two different stereoisomeric forms. The different isomers can have significantly different bioactivities. The letters “D” and “L” associated with the various amino acids refer to their stereoisomeric form.

At the time the application for underlying the original ‘226 patent was filed, and until well after that patent was issued, it was universally believed in the art that the asparagine (Asn) amino acid in daptomycin was the L-isomer.

Years after the issuance of the ‘226 patent and after the reissue application for the ’071 patent was filed, Lilly researchers discovered that daptomycin actually contains the D-isomer of asparagine instead of the L-isomer.

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In 2007, Cubist requested a Certificate of Correction from the PTO, pursuant to 35 U.S.C. 255. That statute reads:

35 U.S.C. 255 Certificate of correction of applicant's mistake.

Whenever a mistake of a ***clerical*** or ***typographical*** nature, or of ***minor character***, which was not the fault of the Patent and Trademark Office, appears in a patent and a showing has been made that such mistake occurred in good faith, the Director may … issue a certificate of correction, ***if the correction does not involve such changes in the patent as would constitute new matter or would require reexamination***. Such patent, together with the certificate, shall have the same effect and operation in law on the trial of actions for causes thereafter arising as if the same had been originally issued in such corrected form.

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In contrast, the reissued statute – i.e., 35 U.S.C. 251 – reads (in part):

35 U.S.C. 251 Reissue of defective patents.

Whenever any patent is, through error without any deceptive intention, deemed wholly or partly inoperative or invalid, ***by reason of a defective specification or drawing***, or by reason of the patentee claiming more or less than he had a right to claim in the patent, the Director shall … reissue the patent for the invention disclosed in the original patent, and in accordance with a new and amended application …. No new matter shall be introduced into the application for reissue.

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No reissued patent shall be granted enlarging the scope of the claims of the original patent unless applied for within two years from the grant of the original patent.

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Cubist explained the mistake in the patent as follows: “the patentees erred in describing one amino acid’s stereochemistry as ‘L-Asn’ in the tail of the compound illustrated in Formula 3, when the correct stereochemistry of the disclosed and claimed amino acid is ‘D-Asn’.”

Formula (3) is repeated in the next slide:

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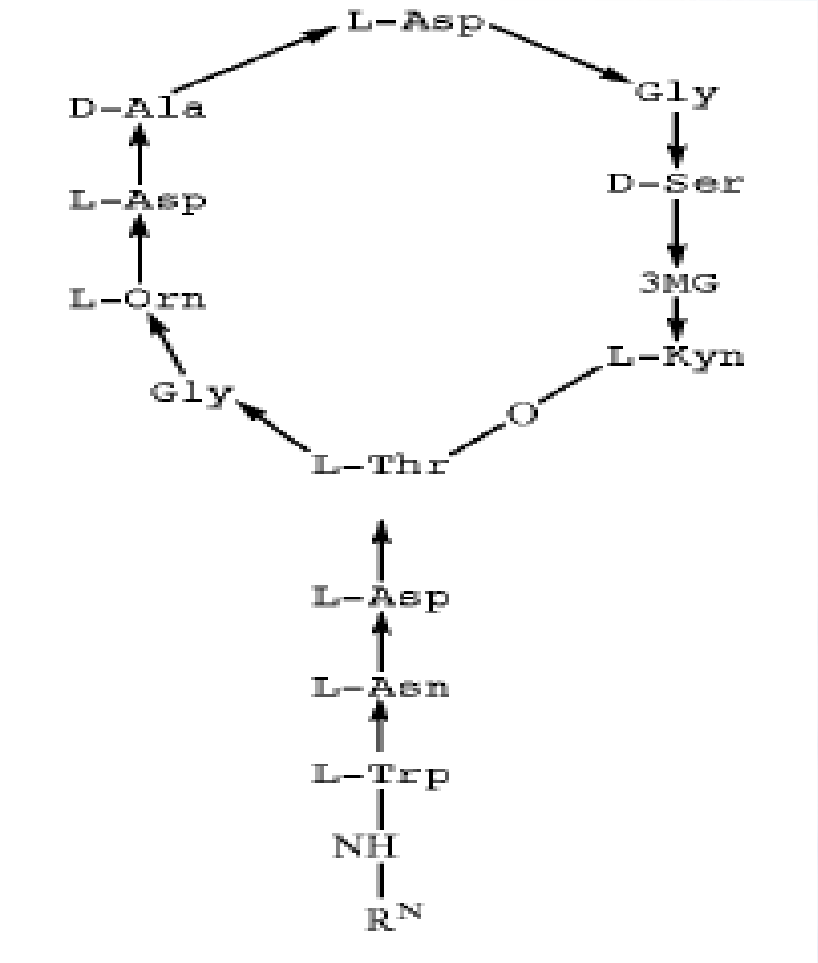

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Cubist indicated that the true nature of the stereochemistry of daptomycin was disclosed in a 2005 journal article by Vivian Miao *et al*. The Miao *et al*. Article "demonstrates that the A-21978C factors of Formula 3 inherently contain the 'D-Asn' in the tail portion illustrated in Formula 3 when isolated from their native source, not an 'L-Asn'."

Based upon this, the Examiner issued a Certificate of Correction – shown in the next slide – correcting Formula 3 in the specification and in four claims by substituting "D-Asn" for "L-Asn" in Formula 3.

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : RE 39,071 E
APPLICATION NO. : 09/547357
DATED : April 18, 2006
INVENTOR(S) : Baker et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In Column 7, Formula 3, the portion of the formula reading "L-Asn" at line 18 should read --D-Asn--.

In Column 16, Formula 3 of claim 18, the portion of the formula reading "L-Asn" at line 62 should read --D-Asn--.

In Column 19, Formula 3 of claim 20, the portion of the formula reading "L-Asn" at line 22 should read --D-Asn--.

In Column 21, Formula 3 of claim 26, the portion of the formula reading "L-Asn" at line 60 should read --D-Asn--.

In Column 25, Formula 3 of claim 30, the portion of the formula reading "L-Asn" at line 20 should read --D-Asn--.

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- In the district court, Hospira argued that the PTO should not have issued the Certificate of Correction, because the change in structural Formula 3 altered the substance of the claims, broadening their reach.

- Hospira argued that the ‘071 patent should be construed to be limited to the variant of the daptomycin compound containing the L-isomer of asparagine.

The compound with the L-isomer of asparagine is actually an antibiotic. However, the antibiotic containing L-Asn is much less potent than daptomycin (which contains D-Asn instead of L-Asn).

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Cubist provided expert testimony that the specification of the patent made it clear that the claims were directed to daptomycin, not to the variant containing the L-isomer of asparagine.

Cubist argued that, because is was clear that the claims of the ‘071 patent were directed to daptomycin (and not to the variant containing the L-isomer of asparagine), it was appropriate for the PTO to correct the error in the structural formula in a Certificate of Correction.

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The district court acknowledged that the chemical structure of Formula 3 in the corrected version of the ‘071 patent is different from that of the pre-correction version. However, the court took the position that the PTO had simply corrected an error in structural Formula 3, without changing the scope of the patent.

The district court agreed with Cubist that the specification make it clear that the claims of the patent were referring to daptomycin all along, and that the pre-correction version merely misidentified the stereoisomer of the asparagine amino acid found in that compound.

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The district court ruled that the specification as a whole "confirms that the Formula 3 compound identified in the claims is truly D-asparagine daptomycin, the byproduct of the fermentation process" described in the specification.

The court held that, accordingly, substituting L-asparagine for D-asparagine in the Formula 3 chemical structure constituted "a correction of minor character because it did not result in 'the new version cover[ing] territory the old one did not'."

Contrary to Hospira's contention, the district court asserted that "D-asparagine was covered both before and after correction."

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Hospira argued against the appropriateness of the Certificate of Correction on three grounds:

- The error being corrected was not a minor error.
- The specification did not comply with the ‘written description’ requirement for the corrected claim.
- Granting the Certificate of Correction violated the ‘recapture’ rule.

Cubist v. Hospira – not minor error

In its appeal to the Federal Circuit, Hospira argued that the change made to the '071 patent by the Certificate of Correction was not a change "of minor character" as required by 35 U.S.C. § 255, because it broadened the scope of the claims in question.

Hospira cited *Superior Fireplace Co. v. Majestic Prods. Co*., 270 F.3d 1358 (Fed Cir. 2001), which had indicated that "A mistake that, if corrected, would broaden the scope of a claim must … be viewed as highly important and thus cannot be a mistake of 'minor character'."

In Hospira's view, the Certificate of Correction was invalid because the change from L-Asn to D-Asn in the structural formula broadened the scope of the claims to read on daptomycin rather than on the L-Asn variant of daptomycin.

Cubist v. Hospira – not minor error

The Federal Circuit indicated that "Contrary to Hospira's argument, the original structural diagram in the '071 patent did not establish that the patent was directed to a compound other than daptomycin. As this court has noted, a chemical structure is 'simply a means of describing a compound; it is not the invention itself.' [citation omitted] In determining what compound the patent claims were directed to, … the specification as a whole must be considered."

The Federal Circuit went on to point out that disclosure in the application taught that daptomycin is obtained through fermentation of *Streptomyces roseosporus*. "That fermentation process necessarily results in daptomycin, not the variant with the L-isomer of asparagine."

Cubist v. Hospira – not minor error

The Federal Circuit went on to say that "… at the time of the original application that matured into the '226 patent [which was reissued as the '071 patent], it was universally believed that the asparagine amino acid in daptomycin was the L-isomer of asparagine, not the D-isomer. It was not until well after the filling of the original '226 patent … and the filing of the reissue application (in 2000) that Lilly researchers determined that the previous understanding of the structure of daptomycin was mistaken …."

The Federal Circuit held that "Even though researches had previously been mistaken about the precise chemical structure of daptomycin, it was nonetheless clear from the specification that the patentees possessed daptomycin (with the D-isomer of asparagine) and that the references to Formula 3 in the claims of the '071 patent were directed to daptomycin."

Cubist v. Hospira – not minor error

The Federal Circuit distinguished the situation in this case from the situation in its earlier decision in *Bayer v. Dow Agrosciences LLC*, 728 F.3d 1324 (Fed. Cir. 2013).

The patentee in *Bayer* claimed a recombinant gene comprising a DNA sequence encoding for a polypeptide having the biological activity of 2,4-D mono-oxygenase. It had been determined before Bayer's patent issued that the gene actually encoded for an enzyme which was a di-oxygenase, not a mono-oxygenase. However, Bayer did not seek to change the claim language to correct the error. Instead, Bayer argued that the claim language should be interpreted to cover any DNA sequence that codes for an enzyme which alters a common herbicide known as "2,4-D" by cleaving its side chain, regardless of whether the cleaving enzyme is a mono-oxygenase or a di-oxygenase.

Cubist v. Hospira – not minor error

The Federal Circuit pointed out that it had "… rejected that argument as a matter of claim construction."

"In this case, unlike in *Bayer*, the applicants sought a certificate of correction to correct the structural diagram, which was based on a previous misunderstanding of the chemical structure of the claimed compound. … the PTO and the district court concluded that the reference to the L-isomer of asparagine was an error and that the claimed compound was the compound with the D-isomer of asparagine. In *Bayer*, by contrast, the patentee sought a broad, functional claim construction based on the original claim language."

Cubist v. Hospira – not minor error

The Federal Circuit held that, “Given the very different approaches employed by the patentees in the two cases, as well as the strong indications in the specification of the ‘071 patent that Formula 3 was in fact daptomycin (despite the error in the structural diagram), the outcome of this case is not controlled by *Bayer*.”

“… we uphold the district court’s conclusion that the certificate of correction did not alter the scope of the patent, but merely corrected an error as to the chemical structure of daptomycin.”

Cubist v. Hospira – no written description

Hospira also contended that the written description requirement was not satisfied, because the specification did not disclose the features or structure of daptomycin (containing the D-isomer of asparagine), and thus the specification provided no indication that the inventors knew they were working with daptomycin having that structure.

The Federal Circuit asserted that “The references in the specification to the ‘A21978C cyclic peptide,’ and to LY146032, Lilly’s codename for daptomycin, would have demonstrated to a person of skill in the art that the inventors were in possession of daptomycin, the product of the fermentation of *Streptomyces roseosporus*, in spite of the error in the structural diagram.”

Cubist v. Hospira – no written description

Hospira relied upon *In re Wallach*, 378 F.3d 1330 (Fed. Cir. 2004) in support of its written description argument.

The Federal Circuit indicated that *Wallach* had little in common with the present situation. “In Wallach, the applicants were in possession of only about 5% of the amino acids of the nucleic acid encoding a particular protein, but they sought to claim all DNA molecules that would code for the protein. That is, they claimed the entire nucleotide sequence of any DNA molecule that would code for the protein, even though they were in possession of only a small portion of one such nucleotide sequence. … applicants had not shown ‘that there is any known or disclosed correlation between the combination of a particular structure of a protein, the protein’s biological activity, and the protein’s molecular weight, on the one hand, and the structure of the DNA molecule encoding the protein on the other’.”

Cubist v. Hospira – no written description

The Federal Circuit went on to say that "In this case, the applicants claimed only what they had produced – the daptomycin molecule – which they identified in several ways. … the identification of the molecule in the specification was sufficient to inform a person skilled in the art that the inventors were in possession of the daptomycin molecule, even though the structure that they ascribed to it was inaccurate in one respect. The description of the molecule provided in the specification in this case was far greater than the very limited description of the DNA sequence in the *Wallach* case, and the claims in this case, unlike those at issue in *Wallach*, were limited to the compound itself."

The Federal Circuit upheld the district court's finding that the asserted claims were not invalid for lack of adequate written description.

Cubist v. Hospira – recapture

Hospira argued that the claims in question were invalid because they violate the "recapture rule" which is applicable to reissued patents – contending that the claims of the reissued '071 patent are impermissibly broader than the corresponding original claims of the '226 patent.

The Federal Circuit indicated that the recapture rules applies if (1) the reissued claims are broader than the original patent claims and (2) the broader aspect of the reissued claims relates to subject matter which was surrendered during prosecution of the original patent. "Moreover, the recapture rule applies only if the patentee surrendered subject matter in the original prosecution in order to overcome a prior art rejection. *In re Clement*, 131 F.3d at 1469."

Cubist v. Hospira – recapture

"… the evidence shows that the applicants did not surrender subject matter in the prosecution of the '226 patent to avoid prior art. In the course of the prosecution …, the examiner rejected claim 24 … on indefiniteness grounds. In response …, the applicants cancelled claim 24. Although the applicants stated that claim 24 was nonobvious, that statement was made in the context of an argument that a large number of the claims of the application … were nonobvious. The applicants did not cancel the other claims, but they cancelled claim 24, which was the only claim rejected on indefiniteness grounds. The applicants ultimately succeeded in overcoming the obviousness objection to the other claims. The prosecution history thus makes it clear that the applicant withdrew claim 24 from the application because of the indefiniteness rejection, not to avoid prior art. Accordingly, the recapture rule does not …" apply.

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CONCLUSION:

Even a serious error in both the specification and claims

– such as an error in a structural formula used to define a chemical compound recited in the claims –

can be corrected via Certificate of Correction procedure

(rather than requiring the use of reissue procedure),

if you can make a case that the scope of the claims is not changed by the correction.

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