United States Court of Appeals for the Federal Circuit

WUHAN HEALTHGEN BIOTECHNOLOGY CORP.,
Appellant

v.

INTERNATIONAL TRADE COMMISSION,
Appellee

VENTRIA BIOSCIENCE INC.,
Intervenor

2023-1389

Appeal from the United States International Trade Commission in Investigation No. 337-TA-1238.

Decided: February 7, 2025

ERIK R. PUKNYS, Finnegan, Henderson, Farabow, Garrett & Dunner, LLP, Washington, DC, argued for appellant. Also represented by J. MICHAEL JAKES, RYAN VALENTINE MCDONNELL, ELIZABETH NIEMEYER, JASON LEE ROMRELL; MICHAEL KUDRAVETZ, Boston, MA.

RONALD TRAUD, Office of the General Counsel, United States International Trade Commission, Washington, DC, argued for appellee. Also represented by DOMINIC L. BIANCHI, WAYNE W. HERRINGTON.

THOMAS P. HENEGHAN, Husch Blackwell LLP, Madison, WI, argued for intervenor. Also represented by JENNIFER E. HOEKEL, St. Louis, MO; BEAU JACKSON, Kansas City, MO; MATTHEW KAMPS, Chicago, IL.

Before MOORE, *Chief Judge*, CHEN, *Circuit Judge*, and MURPHY, *District Judge*.[1]

MOORE, *Chief Judge*.

Wuhan Healthgen Biotechnology Corp. (Healthgen) appeals a final determination from the International Trade Commission (Commission) finding (1) Healthgen's clinical grade albumin products infringe claims 1 and 11–13 of U.S. Patent No. 10,618,951; and (2) Intervenor Ventria Bioscience Inc. (Ventria) satisfied the economic prong of the domestic industry requirement under subparagraph (a)(3) of 19 U.S.C. § 1337 (Section 337). Because substantial evidence supports the Commission's findings, we affirm.

BACKGROUND

Cell culture media supplies essential nutrients for cells to grow in an artificial environment. This media often contains albumin, a protein produced in an animal's liver, which raises contamination and ethical concerns. As a result, recombinant albumin has been used as an alternative. Recombinant technology involves inserting a gene of interest into a host cell to produce a desired protein the cell would not normally produce, allowing for large-scale production of proteins without relying on animal sources.

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[1] Honorable John F. Murphy, District Judge, United States District Court for the Eastern District of Pennsylvania, sitting by designation.

Ventria owns the '951 patent, which is directed, in part, to cell culture media containing recombinant human serum albumin (rHSA) produced in a genetically modified plant. '951 patent at 31:37–41, 39:11–13. Claim 1 is representative and recites:

> 1. A cell culture media supplement or complete media composition for improving the growth of a cell in cell culture comprising:
>
> a recombinant mammalian albumin wherein said albumin is:
>
> i) produced in a transgenic plant;
>
> ii) has less than 1 EU of endotoxin/mg of albumin; and
>
> iii) *less than 2% aggregated albumin*.

Id. at 123:44–51 (emphasis added).

Healthgen imports clinical and medium grade rHSA products. Ventria filed a complaint with the Commission alleging Healthgen's importation activities violated § 337 because its imported products infringed the '951 patent. Ventria relied on its six rHSA products—Cellastim, Exbumin, OptiPEAK, OptiVERO, ITSE+A, and Optibumin—to satisfy the economic prong of the domestic industry requirement and asserted all six products practice the '951 patent.

The Commission instituted an investigation, and the Administrative Law Judge (ALJ) issued an initial determination finding Healthgen violated § 337 by importing clinical and medium grade rHSA products that infringe claims 1 and 11–13 of the '951 patent. J.A. 145–68. The ALJ also found Ventria satisfied the domestic industry requirement under subsections (A), (B), and (C) of § 337(a)(3) based on all six rHSA products and, in the alternative, based on Optibumin alone. J.A. 211–22.

Healthgen petitioned the Commission for review. The Commission affirmed the ALJ's finding of infringement as to Healthgen's clinical grade products, but not its medium grade products. J.A. 25–53. The Commission affirmed the ALJ's finding that Ventria satisfied the domestic industry requirement based on Optibumin alone without further analysis, but took no position on Ventria's five other rHSA products. J.A. 54–55.

Healthgen appeals. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(6).

DISCUSSION

I. Infringement

We review the Commission's legal conclusions de novo and its factual findings for substantial evidence. *Roku, Inc. v. Int'l Trade Comm'n*, 90 F.4th 1367, 1372 (Fed. Cir. 2024). Infringement is a question of fact. *Kinik Co. v. Int'l Trade Comm'n*, 362 F.3d 1359, 1361 (Fed. Cir. 2004).

The Commission found[2] Healthgen's clinical grade products infringe the '951 patent because they contain less than 2% aggregated albumin. J.A. 17–19, 27–32. The Commission relied on Healthgen's SEC-HPLC[3] data, which show the products had at most 1.1% aggregated albumin. J.A. 3371–72.

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[2] We refer to the findings on review in the Infringement and Domestic Industry sections as those of the Commission, whether made by the ALJ or the Commission, because the Commission adopted the ALJ's findings not inconsistent with the Commission's opinion. J.A. 4.

[3] SEC-HPLC (Size Exclusion Chromatography High Performance Liquid Chromatography) is a technique used to separate proteins based on their size. J.A. 17.

Healthgen argues the Commission erred in relying on SEC-HPLC data because the data does not reflect aggregated albumin levels at the time of importation. Appellant's Br. 44–51. Rather, the data, measured in China one day after manufacture, reflects when aggregated albumin is lowest and fails to account for increased aggregation during storage and shipping such that the products are no longer infringing upon importation. *Id.*

The Commission's finding is supported by substantial evidence. It is undisputed SEC-HPLC is a reliable and appropriate test to measure aggregation levels and the measured 1.1% aggregated albumin meets the "less than 2% aggregated albumin" claim limitation. Appellant's Br. 12, 48; Appellee's Br. 16. The Commission found aggregated albumin levels in Healthgen's products do not increase above 2% during storage and shipping. J.A. 29–30, 36–37; J.A. 161. This finding is supported by expert testimony that neither storage alone nor shipment according to common practice would induce additional aggregation, J.A. 1453 at 452:5–16, peer-reviewed literature discussing aggregation increase under extreme stressor conditions, J.A. 3380, and Healthgen's communications to customers explaining stability test results show its products remain stable under its storage and shipping practices, *see, e.g.*, J.A. 3137–39; J.A. 5035; J.A. 7029.

Healthgen contends the peer-reviewed literature suggests aggregation is caused by storage and shipping, and its communications to customers are about stability and quality which are untethered to the "less than 2% aggregated albumin" limitation. Appellant's Br. 46–47, 49–50. Even accepting Healthgen's claim that aggregated albumin levels do increase, Healthgen did not show this aggregation would rise to noninfringing levels before importation. Appellant's Br. 48–49 (claiming aggregated albumin increased to greater than 2%, despite acknowledging "it is unclear precisely how much it had increased upon the product's arrival in the United States"). Healthgen's most

concrete evidence for increased aggregated albumin is comparing SEC-HPLC data taken in September 2020 with Reducing SDS-PAGE[4] data taken in June 2021. *Id.*; *compare* J.A. 3372, *with* J.A. 3297. The same batch that measured 1.1% aggregated albumin in China using SEC-HPLC measured 1.81% nine months later in the United States using Reducing SDS-PAGE. J.A. 3372; J.A. 3297. However, the Reducing SDS-PAGE data is not inconsistent with a finding that the imported products are infringing because 1.81% aggregated albumin still meets the "less than 2% aggregated albumin" limitation. There is thus substantial evidence for the Commission's finding of noninfringement. *Spansion, Inc. v. Int'l Trade Comm'n*, 629 F.3d 1331, 1344 (Fed. Cir. 2010) ("[We] must affirm a Commission determination if it is reasonable and supported by the record as a whole, even if some evidence detracts from the Commission's conclusion." (quoting *Nippon Steel Corp. v. United States*, 458 F.3d 1345, 1352 (Fed. Cir. 2006) (internal quotation marks omitted))).

The Commission also relied on Reducing SDS-PAGE data as an alternative basis for finding infringement. J.A. 19–25, 32–36. Because we affirm the finding of infringement based on SEC-HPLC data, we need not reach the Commission's alternative basis.

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[4] Similar to SEC-HPLC, Reducing SDS-PAGE (Sodium Dodecyl Sulfate Polyacrylamide Gel Electrophoresis) is a technique used to separate proteins based on their size. J.A. 19–20. But unlike SEC-HPLC, Reducing SDS-PAGE alters the sample before analysis by first using a surfactant (SDS) to denature the proteins and then using a reducing agent to break the disulfide bonds holding protein subunits together. J.A. 20, 24.

II. Domestic Industry

Whether the domestic industry requirement is satisfied "typically presents issues of both law and fact." *John Mezzalingua Assocs., Inc. v. Int'l Trade Comm'n*, 660 F.3d 1322, 1327 (Fed. Cir. 2011). Whether investments are "substantial" enough to satisfy this requirement is a question of fact. *Id.* We review the Commission's substantiality finding for substantial evidence. *Roku*, 90 F.4th at 1372.

To demonstrate a patent infringement-based violation of § 337, a complainant must show "an industry in the United States, relating to the articles protected by the patent . . . exists or is in the process of being established." 19 U.S.C. § 1337(a)(2). This domestic industry requirement has a technical prong and an economic prong. *InterDigital Commc'ns, LLC v. Int'l Trade Comm'n*, 707 F.3d 1295, 1298 (Fed. Cir. 2013). Healthgen conceded Optibumin practices the '951 patent and thus satisfies the technical prong. Appellant's Br. 64; J.A. 54. The economic prong considers whether "there is in the United States, with respect to the articles protected by the patent, . . . (A) significant investment in plant and equipment; (B) significant employment of labor or capital; or (C) substantial investment in its exploitation, including engineering, research and development, or licensing." 19 U.S.C. § 1337(a)(3). Only one of subsections (A), (B), or (C) needs to be satisfied to meet the economic prong. *Roku*, 90 F.4th at 1370 n.1. A "quantitative analysis" is required to determine whether investments are "significant." *Lelo Inc. v. Int'l Trade Comm'n*, 786 F.3d 879, 883 (Fed. Cir. 2015).

The Commission found Ventria's Optibumin investments in plant and equipment costs under subsection (A), labor costs under subsection (B), and research and development costs under subsection (C) are significant and substantial because, *inter alia*, 100% of those investments occur in the United States. J.A. 54; J.A. 219–20. A sales-based allocation method was used to calculate the

investments under each subsection. J.A. 211–12. The Commission also found Ventria's Optibumin investments are significant and substantial based on a comparison of the investments to Optibumin's revenue. J.A. 54; J.A. 220. Healthgen argues Ventria's Optibumin investments are too small to be significant or substantial under § 337(a)(3), and low Optibumin revenue, when coupled with small investments, artificially creates high investment-to-revenue ratios. Appellant's Br. 64–73.

The Commission's findings are supported by substantial evidence. That it may have been relatively inexpensive for Ventria to develop and produce its patented product does not alone preclude a finding that Ventria did in fact establish a domestic industry in that product. It is undisputed all of Ventria's investments and activities related to researching, developing, and commercially producing Optibumin occurred within the United States. Appellant's Br. 68–69; Appellee's Br. 36–37. Comparing the cost of foreign to domestic manufacturing to determine the percentage of additional value created by domestic Optibumin operations in the final product yields a value added of 100%. J.A. 219–20. The investment-to-revenue ratio can indicate whether an investment is significant and substantial. A high ratio signals the company is investing heavily in the industry despite comparatively low revenue, highlighting the industry's importance and value to the company, which can be predictive of a significant market. *See, e.g.*, J.A. 1699 at 697:5–17; J.A. 220–21.

Healthgen contends the Commission relies on qualitative factors to overcome Ventria's quantitatively small Optibumin investments in violation of our precedent. Appellant's Br. 64–65, 67–69; *see also Lelo*, 786 F.3d at 885 ("Qualitative factors cannot compensate for quantitative data that indicate insignificant investment and employment."). We do not agree. In *Lelo*, we recognized the comparison of domestic investments to total (i.e., domestic plus foreign) investments as a valid quantitative analysis for

assessing the significance of investments. 786 F.3d at 883–84 (citing *Certain Concealed Cabinet Hinges and Mounting Plates*, Inv. No. 337-TA-289, 1990 WL 10608981, Comm'n Op. at 11–12 (Jan. 8, 1990)). We also recognized the value added by domestic operations as a quantitative factor in the assessment. *Id.* at 884 (citing *Certain Male Prophylactic Devices*, Inv. No. 337-TA-546, USITC Pub. 4005, Comm'n Op. at 24–26 (June 21, 2007)).

Small market segments can still be significant and substantial enough to satisfy the domestic industry requirement. A finding of domestic industry cannot hinge on a threshold dollar value or require a rigid formula; rather, the analysis requires a holistic review of all relevant considerations that is very context dependent. *Bally/Midway Mfg. Co. v. Int'l Trade Comm'n*, 714 F.2d 1117, 1123 (Fed. Cir. 1983) ("There is nothing in the statute which requires that an industry must be of any particular size." (cleaned up)); *Certain Printing and Imaging Devices*, Inv. No. 337-TA-690, 2011 WL 1303160, Comm'n Op. at 27 (Feb. 17, 2011) (explaining whether investment activities are significant or substantial "is not evaluated according to any rigid mathematical formula," but rather requires "an examination of the facts in each investigation, the article of commerce, and the realities of the marketplace"); 134 CONG. REC. S10711-01, 1988 WL 174536 (Aug. 3, 1988) ("Smaller businesses should not be denied the right to seek relief merely because they may have made smaller financial investments than large companies . . . ."). Though the dollar amounts of Ventria's Optibumin investments are small, the Commission found all of the investments are domestic, all market activities occur within the United States, and the high investment-to-revenue ratios indicate this is a valuable market. J.A. 219–21. Under these circumstances, there is substantial evidence for the Commission's finding that the domestic industry requirement is satisfied.

CONCLUSION

We have considered Healthgen's remaining arguments and find them unpersuasive. For the reasons given above, we affirm.

AFFIRMED