IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ENZO LIFE SCIENCES, INC.	
Plaintiff,	**Civil Action No.**
v.	**JURY TRIAL DEMANDED**
HOLOGIC, INC.,	
Defendant.	

COMPLAINT

Plaintiff Enzo Life Sciences, Inc. ("Enzo"), for its Complaint against Defendant Hologic, Inc. ("Hologic") hereby alleges as follows:

PARTIES

1. Plaintiff Enzo is a New York corporation with its principal place of business at 10 Executive Boulevard, Farmingdale, NY 11735.

2. Defendant Hologic is a Delaware corporation with its principal place of business at 35 Crosby Drive, Bedford, MA 01730.

NATURE OF THE ACTION

3. This is a civil action for infringement of United States Patent No. 6,221,581 ("the '581 Patent" or "the Patent-In-Suit") under the Patent Laws of the United States, 35 U.S.C. § 1 *et seq.*

JURISDICTION AND VENUE

4. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

5. This Court has personal jurisdiction over Hologic because, among other things, Hologic has committed, aided, abetted, contributed to, and/or participated in the commission of patent infringement in this judicial district and elsewhere that led to foreseeable harm and injury to Enzo. Moreover, Hologic is a Delaware corporation which, having availed itself of Delaware's corporate laws, is subject to personal jurisdiction in Delaware.

6. This Court also has personal jurisdiction over Hologic because, among other things, Hologic has established minimum contacts within the forum such that the exercise of jurisdiction over Hologic will not offend traditional notions of fair play and substantial justice. Moreover, Hologic has placed products that practice the claimed inventions of the Patent-In-Suit into the stream of commerce with the reasonable expectation and/or knowledge that purchasers and users of such products were located within this District. Hologic has sold, advertised, marketed, and distributed products in this District that practice the claimed inventions of the Patent-In-Suit.

7. Venue is proper in this district pursuant to 28 U.S.C. §§ 1391 and 1400(b).

BACKGROUND OF THE TECHNOLOGY AND THE PATENT-IN-SUIT

8. United States Patent No. 6,221,581, ("the '581 Patent") entitled "Processes for Detecting Polynucleotides, Determining Genetic Mutations or Defects in Genetic Material, Separating or Isolating Nucleic Acid of Interest from Samples, and Useful Compositions of Matter and Multi-hybrid Complex Compositions," was duly and legally issued by the United

States Patent and Trademark Office on April 24, 2001. A copy of the '581 Patent is attached hereto as Exhibit 1.

9. The inventions of the '581 Patent originated from Enzo's pioneering work in the field of molecular genetics in the early 1980s. Molecular genetics is the study of genes and genetic material at the molecular level.

10. At the molecular level, genes are sequences of genetic material. They are important because certain variations and combinations of genes are known to have a role in causing diseases and other conditions.

11. Genetic materials include deoxyribonucleic acid, or DNA, and ribonucleic acid, or RNA. DNA and RNA are comprised of building blocks called nucleotides. DNA and RNA each typically feature four different kinds of nucleotides, or Watson-Crick bases: adenine (A), cytosine (C), guanine (G), and thymine (T) for DNA and adenine (A), cytosine (C), guanine (G), and uracil (U) for RNA.

12. The linear assembly (or chain) of multiple nucleotides is often referred to as an oligonucleotide or polynucleotide sequence or nucleic acid. A single such assembly is referred to in the art as a strand of nucleic acid. These nucleic acid molecules are often specifically defined by their sequences; *i.e.*, the linear assemblage of A, G, C, and T bases for DNA, or A, G, C, and U bases for RNA.

13. Two strands of nucleic acid can pair by hydrogen bonding with each other forming a double helix structure if the arrangement or sequence of nucleotide bases in each strand is such that enough of those bases can pair with each other.

14. Certain nucleotide bases prefer to pair with each other. T and U pair with A. G pairs with C. Scientists describe this relationship by saying that T (or U) and A are complementary bases; similarly, C and G are complementary bases.

15. The joining or binding of two strands of nucleic acid through Watson-Crick base pairing is called hybridization. Two strands of nucleic acid may hybridize along a portion of their full length, depending on where the sufficiently matching or complementary nucleotide sequences line up on the strands.

16. Nucleic acid detection technology often takes advantage of nucleic acid (DNA or RNA) strands' ability to hybridize under certain conditions based upon the structure of the nucleic acids.

17. Scientists can, for example, detect the presence of a particular nucleic acid sequence of interest by using another nucleotide strand sequence known to correspond (by Watson-Crick base pairing), and therefore bind or hybridize, with the nucleotide sequence of interest.

18. The '581 Patent discloses, among other things, novel processes which are useful for separating or isolating nucleic acids of interest from samples. One such process comprises forming a multi-hybrid complex comprising (1) a nucleic acid strand of interest; (2) a second nucleic acid strand which is fixed or immobilized to a solid support; and (3) a third nucleic acid strand which is capable of forming hybrids with both the nucleic acid of interest (1) and the nucleic acid fixed or immobilized to the solid support (2).

19. For example, claim 158 of the '581 Patent recites:

> A process for separating or isolating a nucleic acid of interest in a sample, the process comprising the steps of:
>
> 1) providing three or more nucleic acid strands:

(a) one or more first nucleic acid strands, each such strand being capable of forming a complex comprising at least two hybrids with at least two other of said nucleic acid strands, one of said at least two other nucleic acid strands being a nucleic acid of interest or a portion thereof or being derived from a nucleic acid of interest;

(b) one or more second nucleic acid strands, each such strand being fixed or immobilized to a solid support or being capable of fixation or immobilization to a solid support, and said one or more second nucleic acid strands being capable of forming at least one hybrid with said one or more first nucleic acid strands (a);

(c) one or more third nucleic acid strands contained in a sample, said third nucleic acid strand comprising a nucleic acid of interest or a portion thereof or being derived therefrom, and said one or more third nucleic acid strands being capable of forming at least one hybrid with said one or more first nucleic acid strands (a);

2) forming a mixture comprising said first and third nucleic acid strands (a) and (c) under hybridizing conditions to form at least one first complex comprising one or more hybrids;

3) capturing or collecting said at least one first formed complex to a solid support, by contacting with one or more second nucleic acid strands (b), thereby separating or isolating said nucleic acid of interest in the sample.

20. Enzo is the sole owner and assignee of the entire right and interest in the ’581 Patent and has the right to sue and recover damages for any current or past infringement of the ’581 Patent.

OVERVIEW OF THE HOLOGIC ACCUSED PRODUCTS

21. Each of the products made and sold by Hologic under the brand names PROGENSA® PCA3, APTIMA®, and PROCLEIX® comprises a capture assay which is used to detect the presence of nucleic acids of interest. Each of those products uses Hologic’s target capture, Transcription-Mediated Amplification (TMA), and Hybridization Protection Assay (HPA) technologies. For example, Hologic instructs the users of those capture assays to perform

the following three steps: (1) sample preparation/target capture, (2) target amplification by TMA, and (3) detection of the amplification products (amplicons) by the HPA. *See, e.g.,* Exhibit 2 (APTIMA® HPV Assay Package Insert) at 3-4; Exhibit 3 (PROGENSA® PCA3 Assay Package Insert) at 3-4; Exhibit 4 (PROCLEIX® ULTRIO® Assay Package Insert) at 2-3.

22. During the sample preparation or target capture step of each assay, a single-stranded nucleic acid of interest is obtained from a sample and hybridized to a "capture oligonucleotide" or "capture oligomer," which Hologic designs to be complementary to a target sequence of interest, resulting in a capture oligomer:target hybrid or complex.

23. Those capture oligomer:target complexes are captured onto magnetic microparticles via hybridization between another region of the capture oligomers and single-stranded oligonucleotides fixed to the magnetic microparticles.

24. The result of the target capture step of Hologic's capture assays is therefore a multi-hybrid complex, which is fixed to a magnetic microparticle and comprises three nucleic acid strands: (1) the nucleic acid of interest (or target), (2) the capture oligomer, and (3) the oligonucleotide fixed on the magnetic microparticles. The multi-hybrid complex comprises two hybrids: (1) the nucleic acid of interest hybridized to a portion of the capture oligomer; and (2) a portion of the capture oligomer hybridized to the oligonucleotide fixed on the magnetic microparticles. The multi-hybrid complexes (that include the nucleic acid sequences of interest) are isolated magnetically. Wash steps are then performed to remove uncaptured elements.

COUNT I

Infringement Of The '581 Patent

25. Paragraphs 1 through 24 are incorporated by reference as if fully stated herein.

26. Hologic, either alone or in conjunction with others, has infringed and continues to infringe, both directly and indirectly, one or more claims of the ’581 Patent, including at least exemplary claim 158, under 35 U.S.C. § 271, either literally and/or under the doctrine of equivalents, by using, offering to sell, selling and/or importing into the United States certain nucleic acid assay products (collectively, “the ’581 Accused Products”), including without limitation all products that used and continue to use Hologic’s target capture technology, for example and without limitation:

a. all PROGENSA® PCA3 products, including without limitation PROGENSA® PCA3 Assays;

b. all APTIMA® products, including without limitation APTIMA® Combo 2 assays, APTIMA® CT assays, APTIMA® GC assays, APTIMA® Trichomonas vaginalis assays, APTIMA® HPV assays, APTIMA® HPV 16 18/45 genotype assays, APTIMA® HCV assays, APTIMA® HCV Qualitative RNA assays, APTIMA® HCV Quant Dx assays, APTIMA® HIV-1 Qualitative RNA assays, APTIMA® HIV-1 Quant Dx assays, APTIMA® Zika Virus assays, APTIMA® HBV Quant assays, and APTIMA® Mycoplasma genitalium assays; and

c. all PROCLEIX® products, including without limitation PROCLEIX®HIV-1/HCV assays, PROCLEIX® WNV (West Nile Virus) assays, PROCLEIX® ULTRIO® assays, PROCLEIX® ULTRIO PLUS® assays, PROCLEIX® ULTRIO ELITE® assays, PROCLEIX® HEV assays, and PROCLEIX® Parvo/HAV assays.

27. For example, Hologic infringes exemplary claim 158 of the ’581 Patent by using, offering to sell, selling and/or importing into the United States the APTIMA® HPV Assay. Use

of the APTIMA® HPV Assay (as shown, for example, in Exhibit 2) requires a process for separating or isolating a nucleic acid of interest in a sample, the process comprising the steps of:

1) providing three or more nucleic acid strands (such as (i) capture oligomers, (ii) HPV mRNA target molecules, and (iii) poly-deoxythymidine molecules that are covalently attached to the magnetic particles):

(a) one or more first nucleic acid strands (such as "capture oligomers"), each such strand being capable of forming a complex comprising at least two hybrids with at least two other of said nucleic acid strands (such as (i) capture oligomer:target hybrids, and (ii) capture oligomer:poly-deoxythymidine hybrids) (*see* Exhibit 2 at 3 ("The capture oligomer:target complex is then captured out of solution by decreasing the temperature of the reaction to room temperature. This temperature reduction allows hybridization to occur between the deoxyadenosine region on the capture oligomer and the poly-deoxythymidine molecules that are covalently attached to the magnetic particles."), one of said at least two other nucleic acid strands being a nucleic acid of interest or a portion thereof or being derived from a nucleic acid of interest (such as "HPV mRNA target molecules"));

(b) one or more second nucleic acid strands, each such strand being fixed or immobilized to a solid support or being capable of fixation or immobilization to a solid support (such as "poly-deoxythymidine molecules that are covalently attached to the magnetic particles"), and said one or more second nucleic acid strands being capable of forming at

least one hybrid with said one or more first nucleic acid strands (a) (such as “the deoxyadenosine region on the capture oligomer”);

(c) one or more third nucleic acid strands contained in a sample, said third nucleic acid strand comprising a nucleic acid of interest or a portion thereof or being derived therefrom (such as “HPV mRNA target molecules”), and said one or more third nucleic acid strands being capable of forming at least one hybrid with said one or more first nucleic acid strands (a) (such as “capture oligomers [which] contain sequences complementary to specific regions of the HPV mRNA target molecules”);

2) forming a mixture comprising said first and third nucleic acid strands (a) (such as “capture oligomers”) and (c) (such as “HPV mRNA target molecules”) under hybridizing conditions to form at least one first complex comprising one or more hybrids (*see* Exhibit 2 at 3 (“During the hybridization step, the sequence-specific regions of the capture oligomers bind to specific regions of the HPV mRNA target molecule.”));

3) capturing or collecting said at least one first formed complex to a solid support, by contacting with one or more second nucleic acid strands (b) (such as “poly-deoxythymidine molecules that are covalently attached to the magnetic particles”), thereby separating or isolating said nucleic acid of interest in the sample (*see* Exhibit 2 at 3 (“The capture oligomer:target complex is then captured out of solution by decreasing the temperature of the reaction to room temperature. This temperature reduction allows hybridization to occur between

the deoxyadenosine region on the capture oligomer and the poly-deoxythymidine molecules that are covalently attached to the magnetic particles.")).

28. Each of the '581 Accused Products infringes exemplary claim 158 of the '581 Patent in essentially the same manner described above for the APTIMA® HPV Assay by use of the target capture step. *See, e.g.,* Exhibit 3 at 3-4; Exhibit 4 at 2-3.

29. On information and belief, Hologic has had knowledge of the '581 Patent since at least June 29, 2005 when Hologic's wholly owned subsidiary, Gen-Probe Inc. ("Gen-Probe"), filed an Information Disclosure Statement ("IDS") with the United States Patent and Trademark Office ("PTO"), identifying the '581 Patent as prior art to Gen-Probe's patent application that subsequently issued as United States Patent No. 8,034,554 ("the '554 Patent", attached hereto as Exhibit 5). The '554 Patent relates to methods for separating or isolating target nucleic acids using multi-hybrids to capture the target nucleic acid on a support. *See* Exhibit 5 at abstract ("Methods of the invention separate a target nucleic acid from a sample by using at least one capture probe oligonucleotide that contains a target-complementary region and a member of a specific binding pair that attaches the target nucleic acid to an immobilized probe on a capture support").

30. Gen-Probe also filed an IDS with the PTO identifying the '581 Patent as prior art to Gen-Probe's patent application that subsequently issued as United States Patent No. 8,399,222 ("the '222 Patent", attached hereto as Exhibit 6) on November 25, 2009. The '222 Patent relates to methods for separating or isolating target nucleic acids using multi-hybrids to capture the target nucleic acid on a support. *See* Exhibit 6 at claim 1 ("A multiplex amplification method for specifically detecting the presence of target nucleic acids in a sample comprising the steps of . . .

(c) specifically hybridizing the target hybridizing sequence of the capture probes to a target sequence in their respective target nucleic acids, (d) binding the capture regions to an immobilized probe attached to a capture support by binding together members of a specific binding pair, thereby forming a capture hybrid made up of the miR-221 target nucleic acid, the capture probe and the immobilized probe attached to the capture support, and a capture hybrid made up of the miR-182 target nucleic acid, the capture probe, and the immobilized probe attached to the capture support").

31. Gen-Probe also filed an IDS with the PTO identifying the '581 Patent as prior art to Gen-Probe's patent application that subsequently issued as United States Patent No. 8,551,766 ("the '766 Patent", attached hereto as Exhibit 7) on July 28, 2010. The '766 Patent relates to kits, reaction mixtures and methods for separating or isolating target nucleic acids using multi-hybrids to capture the target nucleic acid on a support. *See* Exhibit 7 at abstract ("Kits, reaction mixtures and methods for separating a target nucleic acid from a sample by using at least one hairpin capture probe oligonucleotide . . . thus forming a capture hybrid that is separated from other sample components before the target nucleic acid is released from the capture support").

32. Gen-Probe also filed an IDS with the PTO identifying the '581 Patent as prior art to Gen-Probe's patent application that subsequently issued as United States Patent No. 8,460,869 ("the '869 Patent", attached hereto as Exhibit 8) on April 14, 2011. The '869 Patent relates to methods for separating or isolating target nucleic acids using multi-hybrids to capture the target nucleic acid on a support. *See* Exhibit 8 at abstract ("Methods of the invention separate a target nucleic acid from a sample by using at least one capture probe oligonucleotide that contains a target-complementary region and a member of a specific binding pair that attaches the target

nucleic acid to an immobilized probe on a capture support, thus forming a capture hybrid that is separated from other sample components").

33. Gen-Probe also filed an IDS with the PTO identifying the '581 Patent as prior art to Gen-Probe's patent application that subsequently issued as United States Patent No. 8,951,730 ("the '730 Patent", attached hereto as Exhibit 9) on March 7, 2013. The '730 Patent relates to compositions and reaction mixtures for separating or isolating target nucleic acids using multi-hybrids to capture the target nucleic acid on a support. *See* Exhibit 9 at 4:8-25 ("Another aspect of the invention is a method of detecting the presence of a target nucleic acid present in a sample that includes the steps of: providing a sample containing a small RNA target nucleic acid . . . mixing the sample with a capture probe that is at least a partially double-stranded structure made up of a first strand and a second strand of nucleic acid, wherein the first strand includes a target hybridizing region and a capture region, and the second strand contains a sequence complementary to a sequence of the first strand, specifically hybridizing the target hybridizing region of the capture probe to a target sequence in the target nucleic acid, binding the capture region to an immobilized probe attached to a capture support, thereby forming a capture hybrid made up of the target nucleic acid, the first strand of the capture probe, and the immobilized probe attached to the capture support, separating the capture hybrid attached to the capture support from other sample components").

34. Hologic has further had knowledge and notice of the '581 Patent in connection with the '581 Accused Products since at least the receipt of a letter dated September 30, 2016 from Enzo to Hologic.

35. Despite its knowledge and notice of the ’581 Patent and its infringement of that patent, Hologic has continued to offer for sale and sell the ’581 Accused Products in the United States. Accordingly, Hologic’s infringement has been and continues to be willful.

36. Hologic has induced infringement, and continues to induce infringement, of one or more claims of the ’581 Patent under 35 U.S.C. § 271(b). Hologic actively, knowingly, and intentionally induced, and continues to actively, knowingly, and intentionally induce, infringement of the ’581 Patent by selling or otherwise supplying the ’581 Accused Products; with the knowledge and intent that third parties will use the ’581 Accused Products supplied by Hologic to infringe the ’581 Patent; and with the knowledge and intent to encourage and facilitate third party infringement through the dissemination of the ’581 Accused Products and/or the creation and dissemination of promotional and marketing materials, supporting materials, instructions, product manuals, and/or technical information related to the ’581 Accused Products.

37. Hologic specifically intended and was aware that the ordinary and customary use of the ’581 Accused Products would infringe the ’581 Patent. For example, Hologic sells and provides the ’581 Accused Products, which when used in their ordinary and customary manner intended by Hologic, infringe one or more claims of the ’581 Patent, including at least exemplary claim 158. Hologic further provides product manuals and other technical information, such as the package inserts attached as Exhibits 2, 3, and 4 to this Complaint, that cause Hologic customers and other third parties to operate the ’581 Accused Products for their ordinary and customary use. Hologic customers and other third parties have directly infringed the ’581 Patent, including at least exemplary claim 158, through the normal and customary use of the ’581 Accused Products. By providing instruction and training to customers and other third parties on how to use the ’581 Accused Products in an infringing manner, Hologic specifically intended to

induce infringement of the ’581 Patent, including at least exemplary claim 158. Hologic accordingly has induced and continues to induce Hologic customers and other users of the ’581 Accused Products to use the ’581 Accused Products in their ordinary and customary way to infringe the ’581 Patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the ’581 Patent.

38. Enzo has been and continues to be damaged by Hologic’s infringement of the ’581 Patent.

39. Hologic’s conduct in infringing the ’581 Patent renders this case exceptional within the meaning of 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Enzo respectfully requests that this Court enter judgment against Hologic as follows:

A. That Hologic has infringed the Patent-In-Suit;

B. That Enzo be awarded damages adequate to compensate Enzo for Hologic’s past infringement and any continuing or future infringement up until the date such judgment is entered, including pre- and post-judgment interest, costs, and disbursements as justified under 35 U.S.C. § 284;

C. That any award of damages be enhanced under 35 U.S.C. § 284 as result of Hologic’s willful infringement;

D. That this case be declared an exceptional case within the meaning of 35 U.S.C. § 285 and that Enzo be awarded reasonable attorney fees;

E. A judgment requiring that, Enzo be awarded a compulsory ongoing licensing fee; and

F. That Enzo be awarded such other and further relief at law or equity as this Court deems just and proper.

DEMAND FOR JURY TRIAL

Plaintiff Enzo hereby demands a trial by jury on all claims and issues so triable.

Dated: October 3, 2016

Respectfully submitted,

Farnan LLP

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