February 14 2018

14-02483-E

US Securities & Exchange Commission
Office of FOIA and Privacy Act Operations
100 F Street, NE Mail Stop 5100
Washington, DC 20549-5100

Dear FOIA Office:

Under the Freedom of Information Act (FOIA), please send a copy of the following:

A copy of: Exhibit 10.81 to the form 10-Q filed by GEN PROBE INC on May 10, 2005

In the event confidential treatment has not expired provide the specific date for which confidential treatment is still in effect. I do not need a copy of the order. We authorize up to $61.00 in processing fees. Thank You,

Paul D'Souza
Editor - Deals

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
STATION PLACE
100 F STREET, NE
WASHINGTON, DC 20549-2465

Office of FOIA Services

March 14, 2018

Mr. Paul D'Souza
Clarivate Analytics
160 Blackfriars Road
London, UK SE18EZ

RE: Freedom of Information Act (FOIA), 5 U.S.C. § 552
Request No. 18-02483-E

Dear Mr. D'Souza:

This letter is in response to your request, dated and received in this office on February 14, 2018, for access to Exhibit 10.81 to the Form 10-Q filed by GEN PROBE INC on May 10, 2005.

In connection with a previous request, we identified and released Exhibit 10.81; as such, we have no objection to releasing this same exhibit to you. No fees have been assessed in this instance.

If you have any questions, please contact me at reidk@sec.gov or (202) 551-3504. You may also contact me at foiapa@sec.gov or (202) 551-7900. You also have the right to seek assistance from Lizzette Katilius as a FOIA Public Liaison or contact the Office of Government Information Services (OGIS) for dispute resolution services. OGIS can be reached at 1-877-684-6448 or Archives.gov or via e-mail at ogis@nara.gov.

Sincerely,

Kay Reid

Kay Reid
FOIA Lead Research Specialist

Enclosure

***Text Omitted and Filed Separately
Confidential Treatment Requested
Under 17 C.F.R. §§ 200.80(b)(4)
And 240.24b-2

Exhibit 10.81

SUPPLY AND PURCHASE AGREEMENT

This Supply and Purchase Agreement ("Agreement"), effective as of the 15th day of February, 2005 (the "Effective Date"), is by and between F. HOFFMANN-LA ROCHE LTD., a Swiss limited liability company with a place of business at Grenzacherstrasse 124, CH-4070 Basle, Switzerland and ROCHE MOLECULAR SYSTEMS, INC., a Delaware corporation with a place of business at 4300 Hacienda Drive, Pleasanton, CA 94588 (collectively, "ROCHE"), and GEN-PROBE INCORPORATED, a Delaware corporation with a place of business at 10210 Genetic Center Drive, San Diego, CA 92121 and its Affiliates (as such term is defined below) (collectively, "GPRO").

BACKGROUND

GPRO requests that ROCHE supply all of GPRO's requirements for HPV Products (as such term is defined below) solely for use with or in HPV TMA Test Kits (as such term is defined below), and ROCHE is willing to supply those requirements all on the terms and subject to the conditions specified in this Agreement.

NOW, THEREFORE, the parties agree as follows:

1. Definitions.

When used in this Agreement, the following terms shall have the meanings set forth below.

1.1 "Affiliates" means, with respect to any Person, any other Person that, directly or indirectly, controls, is controlled by or is under common control with, that Person, provided however, that in each case any such other Person shall be considered to be an Affiliate only during the time period during which such control exists. For purposes of this definition, "control" (including, with correlative meaning, the terms "controlled by" and "under common control with"), as used with respect to any Person, shall mean the possession, directly or indirectly, of the power to direct and/or cause the direction of the management and policies of such Person, whether through the ownership of voting securities, by contract or otherwise. With regard to ROCHE, the term Affiliate shall not include Genentech, Inc., 1 DNA Way, South San Francisco, California 94080-4990, U.S.A. ("Genentech") or Chugai Pharmaceutical Co., Ltd, 1-9 Kyobashi 2-chome, Chuo-ku, Tokyo, 104-8301, Japan ("Chugai").

1.2 "Certificate of Analysis" means the documentation that accompanies the HPV Products and confirms that such products meet the Specifications.

1.3 "Confidential Information" means: (i) any information designated in writing by either party as proprietary or confidential, or if orally disclosed, identified at the time of disclosure as proprietary or confidential and confirmed in writing to be proprietary and confidential within thirty (30) days of disclosure; (ii) ROCHE's business and marketing plans with respect to the HPV Patent Rights and any other intellectual property rights owned by or licensed to ROCHE; and (iii) the terms and conditions of this Agreement and the negotiations between the parties with respect to this Agreement.

1.4 "Days" means calendar days.

1.5 "HPV" means the human papilloma virus.

1.6 "HPV Products" means the HPV Reagent Products and the HPV RNA Transcript and HPV DNA Products.

1.7 "HPV Reagent Products" means certain oligonucleotide reagents manufactured by ROCHE under this Agreement pursuant to the applicable Specifications (as such term is defined below) for use by GPRO in developing the HPV TMA Test Kits and for incorporation by GPRO into the HPV TMA Test Kits (as such term is defined below) all for use only with TMA (as defined below).

1.8 "HPV RNA Transcript and HPV DNA Products" means certain HPV transcripts and/or HPV DNA manufactured by or on behalf of ROCHE under this Agreement pursuant to the applicable Specifications (as such term is defined below) for use by GPRO solely for development, formulation and quality control of the HPV TMA Test Kits (as such term is defined below).

1.9 "HPV TMA Test Kits" means the diagnostic test kits for HPV (inclusive of ASR reagent products) developed and sold by GPRO for use only with TMA, which are designed to run on any current or future instrument appropriate for such purpose.

1.10 "Individual HPV Test Quantity" means that quantity of HPV Reagent Product(s) necessary to generate a diagnostic result for a single patient with respect to one or more types of HPV, as described in the Specifications. Individual HPV Test Quantities shall be reported in appropriate mass units as calculated from the individually measured optical density at 260nm and the extinction coefficient provided to ROCHE by GPRO.

1.11 "Manufacturing Cost" shall mean the fully-burdened cost to ROCHE (expressed on a per unit basis) of manufacturing or having manufactured the HPV Products, together with the packaging thereof, including the cost of materials, direct labor, quality control, and overhead (including royalties paid to Third Parties), all as determined in accordance with ROCHE's standard accounting practices for other

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products manufactured. For the avoidance of doubt, Manufacturing Cost shall not include any cost component attributable to excess or idle manufacturing capacity.

1.12 "Person" shall mean an individual or any legally recognized entity, including any corporation, partnership, limited partnership, limited liability company, association or trust.

1.13 "ROCHE HPV Patents" means certain patent rights owned by or licensed to ROCHE, covering the HPV Products, as further specified in Exhibit A of this Agreement, including all divisionals, continuations, continuations-in-part applications, substitutes, reissues, renewals, re-examinations and extensions of any of the said patent rights, and all patents worldwide issuing on any of the patent applications included within the said patent rights. Additional patent rights developed by ROCHE and, to the extent permitted under the applicable license or acquisition agreement of ROCHE with a third Person, additional patent rights licensed or acquired by ROCHE, directed solely to oligonucleotide probes and methods for their use for the detection of HPV shall also be included within the ROCHE HPV Patents. ROCHE HPV Patents licensed by ROCHE shall be subject to the terms, conditions, limitations and restrictions contained in the applicable license agreement of ROCHE with the third Person.

1.14 "Specifications" means the specifications set forth in Exhibit B of this Agreement, pursuant to which ROCHE shall manufacture the HPV Products under this Agreement, which specifications may be modified from time to time upon request of GPRO, subject to the written consent of ROCHE, such consent not to be unreasonably withheld, conditioned or delayed. ROCHE acknowledges that it is aware that GPRO is likely to request modification of the Specifications from time-to-time in connection with GPRO's development of the HPV TMA Test Kits and prior to any First Commercial Sale thereof.

1.15 "TMA" means "Transcription-Mediated Amplification", a transcription-based process for amplifying a DNA or RNA target source. TMA comprises a substantially continuous and isothermal process of generating multiple RNA copies of the target sequence or its complement. It is expressly understood that the heating of target RNA to relax the molecule prior to the transcription-based process can comprise a step in "TMA." Further, it is expressly understood that a transcription-based process, as described herein, that begins with a single stranded DNA or RNA target sequence or a double stranded DNA target sequence includes no more than two cycles of heat denaturation and primer extension, employs only one primer in the first primer extension step, and produces a double stranded promoter sequence is included within the meaning of "TMA." Finally, it is expressly understood and agreed that the TMA process is not polymerase chain reaction ("PCR") amplification, namely the amplification of a nucleic acid sequence and the complement of that sequence by more than two cycles of denaturation of a double stranded nucleic acid, annealing and extension of two primers, wherein the sequence and its complement are repeatedly separated, each

separated strand serves as a template for primer extension and the resulting double stranded nucleic acid is used in further cycles of denaturation, annealing and extension of primers.

1.16 "Transfer Fee" shall have the meaning provided in Section 3.2, 3.3 or 3.4, as applicable.

2. Supply and Purchase of HPV Products.

2.1 Obligation to Purchase. GPRO shall purchase from ROCHE, upon GPRO's request as provided in this Agreement, all of its requirements of HPV Reagent Products for use in HPV TMA Test Kits and all of its requirements of HPV RNA Transcript and HPV DNA Products for use in connection with HPV TMA Test Kits. GPRO's obligation under this Section 2.1 shall terminate upon any termination of this Agreement pursuant to Section 9.

2.2 Obligation to Supply. ROCHE shall supply all of GPRO's requirements of HPV Reagent Products for use in HPV TMA Test Kits and all of GPRO's requirements of HPV RNA Transcript and HPV DNA Products for use in connection with HPV TMA Test Kits, as requested by GPRO under Section 2.1. ROCHE will manufacture, or have manufactured, the HPV Products in accordance with the Specifications and appropriate Quality Systems Regulations and then current Good Manufacturing Practices (cGMP) controls. Any material deviations from the prescribed ROCHE manufacturing process shall be communicated to GPRO prior to ROCHE's release of the HPV Products. Manufacturing records for the HPV Products will be kept at the facility where such HPV Products were manufactured and will be available for necessary regulatory inspections as provided in Section 6.2.1.

2.3 Scope of GPRO's Rights for HPV Products. GPRO shall utilize HPV Reagent Products purchased under this Agreement solely for development of and incorporation into HPV TMA Test Kits, and for no other purpose. GPRO shall utilize HPV RNA Transcript and HPV DNA Products purchased under this Agreement solely for its own internal development, formulation and quality control of HPV TMA Test Kits, and for no other purpose. GPRO shall not have the right to resell the HPV Products on a standalone basis or as incorporated into any other product, but only as incorporated into HPV TMA Test Kits (including as one component of ASR reagent products). GPRO shall have the unrestricted and unconditional right to incorporate the HPV Reagent Products into the HPV TMA Test Kits and GPRO shall have the unrestricted and unconditional right to use and sell the HPV TMA Test Kits (including to its distributors).

2.4 Restriction on Supply by ROCHE. ROCHE shall not sell or supply the HPV Products manufactured by it under this Agreement to any third Person.

2.5 Failure a Material Breach. Failure by a party to comply with Sections 2.1, 2.2, 2.3 and 2:4 shall constitute a material breach of this Agreement by such party.

3. Fees.

3.1 Manufacturing Access Fee and Additional Charge for Patented Products. In consideration of ROCHE's agreement to manufacture and supply the HPV Products to GPRO under the ROCHE HPV Patents pursuant to this Agreement, GPRO shall pay to ROCHE a non-refundable manufacturing access fee and additional charge for the HPV Products of Thirty Million United States Dollars (US$30,000,000), payable in two installments as follows: (i) Twenty Million United States Dollars (US$20,000,000) within ninety (90) days after the Effective Date; and (ii) Ten Million United States Dollars (US$10,000,000) within the earlier of (A) ten (10) days of GPRO achieving the "First Commercial Sale" of a HPV TMA Test Kit, or (B) December 1, 2008. As used in this Agreement, a "First Commercial Sale" shall mean the first commercial sale by GPRO of any HPV TMA Test Kit (not including any use or transfer for Non-Commercial Use (as defined below) or Clinical Trial Use (as defined below)).

3.2 Transfer Fees for HPV Reagent Products. As additional consideration for ROCHE's agreement to manufacture and supply the HPV Reagent Products to GPRO under this Agreement, GPRO shall pay to ROCHE, for the supply of bulk quantities of the HPV Reagent Products during the term of this Agreement, transfer fees (the "Reagent Transfer Fee") as follows:

3.2.1 Each purchase order submitted by GPRO will ordinarily include each of the HPV Reagent Products to be incorporated into the HPV TMA Test Kits. As to each such order, GPRO shall pay to ROCHE in respect of each Individual HPV Test Quantity of HPV Reagent Products manufactured and sold by ROCHE to GPRO as follows: (i) from the Effective Date until twelve (12) months after GPRO achieves the First Commercial Sale of a HPV TMA Test Kit, US$4.00 per Individual HPV Test Quantity; (ii) for months thirteen (13) to twenty-four (24) after GPRO achieves the First Commercial Sale of a HPV TMA Test Kit, US$3.00 per Individual HPV Test Quantity; (iii) for months twenty-five (25) to thirty-six (36) after GPRO achieves the First Commercial Sale of a HPV TMA Test Kits, US$2.00 per Individual HPV Test Quantity; (iv) for months thirty-seven (37) to forty-eight (48) after GPRO achieves the First Commercial Sale of a HPV TMA Test Kit, US$1.00 per Individual HPV Test Quantity; and (iv) for the remainder of the term of this Agreement, the greater of (A) US$.50 per Individual HPV Test Quantity, or (B) the Manufacturing Cost thereof (or ROCHE's actual incurred cost if manufactured for ROCHE by a third Person), plus a margin of fifty percent (50%), provided however, that for individual orders of GPRO made during such remainder of the term of the Agreement for a lot size of at least three million (3,000,000) Individual HPV Test Quantities per

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order, such Transfer Fee shall not exceed US$1.00 per Individual HPV Test Quantity.

3.2.2 Notwithstanding the fact that each purchase order submitted by GPRO will ordinarily include each of the HPV Reagent Products to be incorporated into the HPV TMA Test Kits, GPRO shall have the right to separately order and purchase from ROCHE one or more individual oligonucleotide reagents included within the HPV Reagent Products. As to each such order, GPRO shall pay to ROCHE a Transfer Fee per Individual HPV Test Quantity of each individual oligonucleotide reagent. Such Transfer Fee shall be equal to the Transfer Fee set forth in Section 3.2.1, above, multiplied by 1/N, where "N" is the total number of distinct oligonucleotide reagents then included within the HPV Reagent Products and incorporated by GPRO into the HPV TMA Test Kits. Nothing contained in this Section 3.2.2 shall diminish GPRO's obligation under Section 2.1 to purchase from ROCHE all of GPRO's requirements of HPV Reagent Products for use in HPV TMA Test Kits.

3.3 Transfer Fees for HPV RNA Transcript and HPV DNA Products. As additional consideration for ROCHE's agreement to manufacture and/or supply the HPV RNA Transcript and HPV DNA Products to GPRO under this Agreement, GPRO shall pay to ROCHE, for the supply of bulk quantities of the HPV RNA Transcript and HPV DNA Products during the term of this Agreement, a transfer fee in respect of such HPV RNA Transcript and HPV DNA Products sold by ROCHE to GPRO (the "Transcript Transfer Fee") equal to ROCHE's Manufacturing Cost, plus a margin of fifty percent (50%), or ROCHE's actual incurred cost if manufactured for ROCHE by a third Person, plus a margin of twenty-five percent (25%), provided however, that if HPV RNA Transcript and HPV DNA Products are manufactured by ROCHE and sold to GPRO, the Transcript Transfer Fee shall not exceed two hundred percent (200%) of the Transcript Transfer Fee that GPRO can reasonably demonstrate would have been charged if ROCHE had alternatively had such HPV Transcript Product manufactured by a third Person for ROCHE for sale to GPRO.

3.4 HPV Reagent Products for Non-Commercial Use. Notwithstanding Section 3.2 of this Agreement, GPRO shall be entitled to purchase a limited quantity of the HPV Reagent Products for "Non-Commercial Use". For the purpose of this Section 3.4, "Non-Commercial Use" shall mean that the intended use of such HPV Reagent Products, as demonstrated by GPRO to ROCHE's reasonable satisfaction, shall be solely for GPRO's internal research and development and not for transfer or sale by GPRO to any third Person. GPRO currently estimates that it will require approximately 4,000,000 Individual HPV Test Quantities for Non-Commercial Use.

3.5 HPV Reagent Products for Clinical Trials. Notwithstanding Section 3.2 of this Agreement, GPRO shall be entitled to purchase a limited quantity of the HPV Reagent Products for use only in those clinical trials required to obtain applicable

governmental regulatory approvals ("Clinical Trial Use"), provided that GPRO shall furnish such HPV Reagent Products (and/or corresponding HPV TMA Test Kits) to the clinical trial researchers or governmental agencies at no charge and shall not sell such HPV Reagent Products (and/or corresponding HPV TMA Test Kits) to any third Person and, provided further, that GPRO may only purchase up to 20,000 Individual HPV Test Quantities of the HPV Reagent Products for use for such purposes, and provided finally, that if GPRO can demonstrate to ROCHE's reasonable satisfaction that additional HPV Test Quantities are reasonably needed by GPRO for such purposes, GPRO may purchase an additional amount of HPV Test Quantities up to a maximum of 80,000 additional Individual HPV Test Quantities for use only for such purposes.

3.6 Transfer Fee and Order Size for Non-Commercial Use and Clinical Trial Use. The Transfer Fee and order size for GPRO's purchase of HPV Reagent Products for Non-Commercial Use and Clinical Trial Use shall be in accordance with Exhibit C to this Agreement. With respect to any Individual HPV Test Quantities ordered by GPRO pursuant to this Section 3.6 that are not used by GPRO for Non-Commercial Use or Clinical Trial Use as provided in Sections 3.4 and 3.5 and are instead reclassified by GPRO for commercial use and incorporation by GPRO into HPV TMA Test Kits, upon the earlier of such reclassification or incorporation into HPV TMA Test Kits, GPRO shall immediately notify ROCHE. GPRO shall concurrently pay ROCHE the difference between the applicable Transfer Fees in effect pursuant to Section 3.2 as of the date of original delivery thereof for such Individual HPV Test Quantities and the applicable price previously paid by GPRO for such Individual HPV Test Quantities as provided in Exhibit C.

3.7 Third Party Royalties. Any royalties or other fees owed by ROCHE to any third Person for the practice of the ROCHE HPV Patents shall be borne exclusively by ROCHE. Any royalties or other fees owed to any third Person for or in connection with the HPV TMA Test Kits or the practice of TMA shall be borne exclusively by GPRO.

3.8 Replacement of Scrapped HPV Reagent Products. During the term of this Agreement, if GPRO demonstrates to ROCHE's reasonable satisfaction that any HPV Reagent Products, ordered by GPRO for incorporation into HPV TMA Test Kits and paid for pursuant to Section 3.2, have been fully and finally scrapped by GPRO due to GPRO internal accidental damage or loss, then ROCHE shall supply replacement HPV Reagent Products and GPRO shall pay ROCHE fifty percent (50%) of the Transfer Fee then in effect but in no event less than the greater of (a) US$.50 per Individual HPV Test Quantity, or (b) the Manufacturing Cost thereof plus a margin of fifty percent (50%). For the avoidance of doubt, this Section 3.8 shall not apply to HPV Reagent Products ordered by GPRO for Non-Commercial Use or Clinical Trial Use.

4. Forecasts and Orders.

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4.1 Forecast. Each calendar quarter, on or about the first day of each quarter, GPRO will provide to ROCHE a rolling forecast of its requirements for HPV Products for the next (12) twelve months, based on GPRO's good faith estimates of anticipated sales of HPV TMA Test Kits. Such forecast shall include good faith estimates of anticipated delivery dates. Failure to provide such information may result in product shortages or delays. GPRO's forecasts shall not be binding.

4.2 Purchase Orders. GPRO shall purchase HPV Products hereunder by issuing a written purchase order identifying the HPV Products to be purchased, the quantity, total order purchase price based on the then applicable Transfer Fees, delivery instructions, delivery dates and any other special information. The delivery date specified in each purchase order shall be at least sixty (60) days after the date of the purchase order when ordering 1 to 5 lots of HPV Reagent Products, ninety (90) days after the date of the purchase order when ordering 6 to 15 lots of HPV Reagent Products and one hundred twenty (120) days after the date of the purchase order when ordering 16 to 25 lots of HPV Reagent Products, provided however, that GPRO recognizes that delivery dates for initial shipments of HPV Products may be longer than the periods set forth in this Section 4.2 and the parties agree to confer and reasonably agree upon reasonable lead times for the delivery of initial shipments of the HPV Products with the goal and intention of achieving lead times as close to one hundred twenty (120) days as possible with commercially reasonable efforts. Except as otherwise provided in Exhibit C, a "lot" of HPV Reagent Product shall be the equivalent of one million Individual HPV Test Quantities and the minimum order for a purchase order shall be one (1) lot and the maximum order for a purchase order shall be 25 lots. Each purchase order shall specifically reference this Agreement. Within seven (7) days of the delivery of each purchase order, as partial pre-payment for the applicable HPV Products, GPRO shall deposit with ROCHE US$0.50 per Individual HPV Test Quantity for the HPV Reagent Products that were the subject of the purchase order and the Transfer Fee pursuant to Section 3.3 for the HPV RNA Transcript and HPV DNA Products that were the subject of the purchase order.

4.3 Acceptance of Purchase Orders. ROCHE may accept or reject purchase orders within seven (7) working days of ROCHE's receipt of written purchase orders. Provided that a purchase order does not request lot quantities of HPV Products greater than 125% of previously forecasted quantities, ROCHE shall accept all purchase orders that are issued in conformance with the provisions of this Agreement. ROCHE shall use commercially reasonable efforts to accommodate lot quantities of HPV Products greater than 125% of previously forecasted quantities. Upon acceptance of a purchase order, such purchase order and acceptance shall constitute a binding contract between GPRO and ROCHE (subject to the terms and conditions of this Agreement).

4.4 Deferral and Cancellation. Prior to the scheduled delivery date specified on a purchase order, GPRO may defer delivery of HPV Products specified in such purchase order for a period not to exceed ninety (90) days, provided however, that

in all cases upon the expiration of such ninety (90) days, ROCHE may deliver the HPV Products and invoice for the applicable amount due. Deferrals related to that purchase order must be by written notice, and shall be subject to a charge of 10% of the unpaid purchase price for the deferred HPV Products for each thirty (30) days deferred based on the Transfer Fee in effect on the date of the purchase order.

4.5 Acceptance or Rejection. GPRO shall inspect all HPV Products within sixty (60) Days of receipt thereof, and may reject any HPV Product that does not conform to the Specifications, provided that it has not been used, abused or damaged by GPRO or GPRO's agents. Any HPV Product not properly and timely rejected by GPRO shall be deemed accepted. To reject an HPV Product, GPRO shall notify ROCHE in writing within sixty (60) Days of receipt of the HPV Product of its rejection and shall promptly return the rejected HPV Product to ROCHE. All returned HPV Products shall be accompanied by suitable documentation, as specified by ROCHE in response to GPRO's notification of rejection. GPRO shall also provide all reasonable assistance to ROCHE to facilitate ROCHE's investigation and confirmation of the non-conformance basis for rejection. After confirmation of the non-conformance basis for rejection, ROCHE shall replace the rejected HPV Product with conforming HPV Product as promptly as reasonably possible and within the periods set forth in Section 4.2. Notwithstanding the foregoing, if GPRO first discovers any non-conforming condition in HPV Products as manufactured by or for ROCHE after the aforementioned 60-day period and such condition would not have been detected in an initial inspection using commercially reasonable inspection methods (a "Latent Defect") and GPRO immediately notifies ROCHE of such non-conforming condition, then such HPV Product shall be deemed to be non-conforming under this Agreement and GPRO shall have all remedies originally available to it under this Section 4.5 with respect to such non-conforming HPV Products.

4.6 Inconsistencies. Notwithstanding the content of GPRO's purchase order. ROCHE's invoice, or any other document submitted by one party to the other, this Agreement shall take precedence over such purchase order or other document, and this Agreement shall govern and control over any conflicting or inconsistent terms of such purchase order(s), invoices(s) or other documents, and all terms which are inconsistent with those provided in this Agreement shall be null and void.

4.7 Product Modifications. Each party will notify the other party promptly (and, in any case, no later than thirty (30) Days) after it receives information that the processes, Specifications or materials used to manufacture the HPV Products will be changed. Without pre-approval by GPRO, which shall not be unreasonably withheld, conditioned or delayed, ROCHE shall not make any change in the manufacturing process for the HPV Products that would cause the HPV Products not to meet the Specifications. The parties shall discuss any such changes and agree on their acceptability and any potential financial impact the changes may

have on the Transfer Fee. Any such agreement shall be in the form of a signed amendment to this Agreement.

5. Packing and Delivery.

5.1 Delivery. ROCHE will use commercially reasonable efforts to effect delivery on or before the date indicated in GPRO's purchase order, provided that date is in conformance with the terms and conditions of this Agreement. ROCHE shall not be liable for any delay or failure in performance or delivery where such delay or failure arises or results from any cause beyond ROCHE's reasonable control, including, but not limited to, strike, boycott, or other labor disputes, failures or delays by common carriers, embargo, governmental regulation, or delay in obtaining materials, earthquakes, storms, power outages or acts of God. In the event of any such delay or failure in performance due to a cause beyond ROCHE's reasonable control, ROCHE shall have such additional time within which to perform its obligations hereunder as may reasonably be necessary in ROCHE's reasonable judgment.

5.2 Delivery Terms. Delivery of HPV Products shall be made by Roche to GPRO at GPRO's designated facility or facilities as is specified in GPRO's purchase order. ROCHE shall invoice GPRO for all transportation charges.

5.3 Packaging. All HPV Products delivered pursuant to this Agreement shall be suitably packed in ROCHE's standard transportation cartons, marked for delivery to the relevant delivery address, and delivered to GPRO as provided herein. ROCHE shall comply with any special packaging requirements set forth in the Specifications. ROCHE shall select the carrier.

5.4 Custody, Control, Title, Risk of Loss and Location of Sale. Control, custody, title and risk of loss with respect to all HPV Products shall pass from ROCHE to GPRO upon delivery of the HPV Products to GPRO at its designated facility. Accordingly, the sale of HPV Products by ROCHE to GPRO shall occur for all purposes of this Agreement upon delivery to GPRO's designated facility. The parties further acknowledge, intend and agree that upon ROCHE's sale of the HPV Products for use in or with the HPV TMA Test Kits that the doctrine of patent exhaustion will apply with respect to such use and as to all claims of the ROCHE HPV Patents. GPRO acknowledges and agrees that following the sale of the HPV Products hereunder GPRO will not transport such HPV Products (including as incorporated into HPV TMA Test Kits) from the jurisdiction in which they were delivered and purchased to any other jurisdiction in which the doctrine of patent exhaustion would not apply to the importation, offer for sale, sale or use thereof based on the original sale and delivery in the first jurisdiction. (By way of example and not of limitation, under current law GPRO acknowledges and agrees that HPV Reagent Products sold to it in the United States will not be transported to, or sold by GPRO in HPV TMA Test Kits in, Europe and GPRO will purchase and take delivery in Europe of all HPV Products to be used in or with HPV TMA Test Kits to be sold in Europe.)

5.5 Disclaimer of Patent Exhaustion or Implied Licenses as to Other ROCHE Patents. In connection with the delivery and sale of HPV Products pursuant to this Agreement, ROCHE hereby disclaims any applicability of the doctrine of patent exhaustion with respect to, or any grant of implied license rights under, any patent rights of ROCHE or its Affiliates other than the ROCHE HPV Patents, and GPRO acknowledges and agrees that it obtains no benefit of the doctrine of patent exhaustion or implied license rights under any other patent rights of ROCHE or its Affiliates.

5.6 Certificate of Analysis. ROCHE shall provide a Certificate of Analysis with each delivery of HPV Products.

6. Invoicing and Payment; Inspections and Audits, Etc.

6.1 Invoicing and Payment. ROCHE will invoice GPRO for the Transfer Fees after ROCHE has delivered the HPV Products. The Transfer Fee to be charged shall be the Transfer Fee in effect pursuant to Section 3.2 on the date the subject HPV Products were delivered to GPRO, less the deposit made by GPRO pursuant to Section 4.2. GPRO shall pay all applicable amounts due in respect of each purchase order within thirty (30) days after receipt of ROCHE's invoice therefor. Payment terms are net thirty (30) Days from receipt of ROCHE's invoice to GPRO. GPRO shall be liable for the invoiced price of all HPV Products substantially conforming to a GPRO purchase order, unless GPRO properly rejected the HPV Products in a timely manner. If payment is not received by the due date, a service charge may be added at the rate of 1.0% per month (12% per year) or the maximum legal rate, whichever is less, to unpaid invoices from the due date thereof, and GPRO agrees to pay such charge. If GPRO consistently fails to make payments when due, ROCHE reserves the right to require alternative payment terms, including, without limitation, sight draft, letter of credit, or payment in advance. Upon making such demand, ROCHE may suspend production and/or deliveries. If, within the period stated in such demand, but in no event longer than thirty (30) Days, GPRO fails to give adequate assurance of due performance, ROCHE may make deliveries under reservation of a security interest and demand payment against tender of documents of title. GPRO hereby represents to ROCHE that GPRO is now solvent and agrees that each acceptance of delivery of HPV Product sold hereunder shall constitute reaffirmation of this representation at such time.

6.2 Inspections and Audits.

6.2.1 GPRO Audits. ROCHE shall permit and assure GPRO access during reasonable business hours and upon thirty (30) days written notice to conduct an audit (i) of those areas of all facilities where the HPV Products are manufactured, tested, filled, released, packaged, labeled, stored and/or handled, as applicable, and (ii) all quality control records, test records and manufacturing records for the

HPV Products, each in order for GPRO to perform a quality assurance audit of such facilities and activities, (iii) ROCHE's qualification policies and procedures for third Person manufacturers and suppliers, and (iv) in the event the Transfer Fee for HPV Products is determined based upon ROCHE's Manufacturing Cost thereof; the cost basis for such Manufacturing Cost, provided, however, that GPRO shall not cause such an audit to occur more than once in any given twelve (12) month period, except as may be required by cGMP or any other applicable law or regulation, and, provided, further, that all such audits shall be conducted in such a manner as to not unreasonably interfere with the conduct of regular business activities at the audited facility. ROCHE shall permit GPRO or a third Person designated by GPRO to copy, under reasonable confidentiality obligations, such documents as GPRO can reasonably establish are required to be copied for regulatory purposes.

6.2.2 GPRO Books and Records. GPRO shall maintain regular and complete records for a period of three (3) years after the expiration of the calendar quarter to which they pertain, sufficient to enable verification of GPRO's compliance with the terms and conditions of this Agreement and the accuracy of all statements and payments made by GPRO. Such records shall be maintained at GPRO's regular place of business and, on thirty (30) days notice, shall be available for inspection and audit by ROCHE's outside accountants, acting in confidence, during normal business hours, for three (3) years immediately following the end of the calendar quarter to which they pertain; provided, however, that ROCHE shall not cause such an inspection and audit to occur more than once in any given twelve (12) month period or with respect to any records after the expiration of three (3) years after the end of the calendar quarter to which such records pertain and, provided, further, that all such inspections and audits shall be conducted in such a manner as to not unreasonably interfere with the conduct of the GPRO's regular business activities. Should any such audit reveal a payment short fall by GPRO, the amount of the short fall shall be paid promptly by GPRO after the discovery thereof, together with interest thereon calculated at the lower of (i) the prime rate of the Bank of America plus two percent (2%), or (ii) the maximum rate provided under applicable law, until paid. If the payment shortfall revealed in any audit is greater than five percent (5%), GPRO shall also pay all costs and expenses of the audit, including all charges of ROCHE's outside accountants.

6.3 Taxes and Duties. The purchase price of all HPV Products is exclusive of any taxes, fees, duties, licenses or levies now or hereinafter imposed upon the production, storage, sale, transportation or use of the HPV Products, and such taxes and items shall be paid by GPRO (other than a tax measured by ROCHE's net income). In lieu of payment, GPRO shall provide an exemption certificate acceptable to the taxing authorities.

7. Label Statement; Patent Marking; Trademarks.

***Confidential Treatment Requested

7.1 Label Statement. GPRO shall include on and with each HPV TMA Test Kit a statement to the effect that the product is sold and intended for use only in Human In Vitro Diagnostics and that all other implied licenses are expressly disclaimed. The location of such label disclaimer shall be on the outside of the packaging for each HPV TMA Test Kit and on any product insert included with the product or otherwise published by GPRO, or such other reasonably prominent location(s) as shall be specified by ROCHE from time to time.

7.2 Patent Marking. ROCHE will mark all HPV Products as appropriate under statutory patent provisions with respect to the ROCHE HPV Patents. GPRO will also mark all HPV TMA Test Kits as appropriate under statutory patent provisions with respect to the ROCHE HPV Patents on both the outside packaging and any product insert included with the product or otherwise published by GPRO as reasonably directed by ROCHE from time to time. With respect to containers of HPV Products included in the HPV TMA Test Kits, if it is reasonably feasible to mark such containers as appropriate under statutory patent provisions, GPRO shall so mark such containers as reasonably directed by ROCHE from time to time, provided, however, that if it is not reasonably feasible to so mark such containers because of the size of the containers or other limiting considerations, GPRO shall include the following statement on the outside of each such container as reasonably directed by ROCHE from time to time: "Patented. See Product Packaging and Insert for Patent Numbers."

7.3 No Trademark Rights. Neither party shall have any license or right to use any trademark owned by or licensed to the other party.

8. Warranties; Exclusions, Disclaimers, Indemnification; Limitation of Liability.

8.1 ROCHE Warranties.

8.1.1 With respect to any HPV Product purchased by GPRO under this Agreement ROCHE warrants that the HPV Product will conform to the applicable Specifications and will be free from defects in materials or workmanship when delivered to GPRO pursuant to the provisions of Section 5 above. ROCHE shall promptly replace all HPV Products that do not conform to this warranty at no charge to GPRO. HPV Products are temperature sensitive, as fully set forth in the Specifications. Subject to the inspection and rejection procedures and remedies set forth in Section 4.5, once HPV Products have been removed from original containers and/or incorporated into the HPV TMA Test Kits, the foregoing warranty no longer applies.

8.1.2 Subject to the provisions and limitations of Section 9.3 below, ROCHE warrants that the execution, delivery and performance of this Agreement

by ROCHE (including the manufacture, use, sale, or offer for sale and importation of the HPV Products by ROCHE pursuant to this Agreement) will not violate or breach any agreement to which ROCHE is a party or is otherwise bound or subject and that the sale of the HPV Products by ROCHE to GPRO is an authorized sale pursuant to any and all such agreements.

8.2 Mutual Warranties. Each party warrants to the other that (i) it is a validly existing corporation in good standing under its jurisdiction of incorporation and has all requisite corporate power and authority to enter into this Agreement and perform its obligations set forth herein, (ii) this Agreement has been duly authorized by all necessary corporate action of such party, and has been duly executed and delivered by it, and (iii) there is no action, suit or governmental, administrative, arbitration or regulatory proceeding pending as of the Effective Date which could prevent such party from carrying out its obligations under this Agreement.

8.3 Exclusion and Disclaimer of Other Warranties.

THE WARRANTIES SET OUT IN SECTIONS 8.1.1, 8.1.2 and 8.2 ARE IN LIEU OF ALL OTHER REPRESENTATIONS OR WARRANTIES, EXPRESSED OR IMPLIED, INCLUDING THOSE OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE OR NON-INFRINGEMENT. ROCHE DISCLAIMS ANY REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, AS TO THE VALIDITY OF THE ROCHE HPV PATENTS OR AS TO WHETHER THE HPV PRODUCTS OR THE HPV TMA TEST KITS WILL BE FREE FROM ANY INFRINGEMENT OF THE INTELLECTUAL PROPERTY RIGHTS OF ANY THIRD PERSON.

8.4 Indemnification.

8.4.1 ROCHE shall indemnify, hold harmless and defend GPRO, its directors, officers, shareholders, employees, representatives, attorneys, Affiliates, licensors and agents (each such Person an "GPRO Indemnitee") from and against any and all claims, suits and damages asserted by any third Person, and all related costs, fees and expenses (including reasonable attorneys' and experts' fees and court costs) suffered or incurred by any GPRO Indemnitee arising out of, resulting from or otherwise concerning any breach of the warranties provided by ROCHE in Section 8.1.2 and 8.2.

8.4.2 GPRO shall indemnify, hold harmless and defend ROCHE, its directors, officers, shareholders, employees, representatives, attorneys, Affiliates, licensors and agents (each such Person an "ROCHE Indemnitee") from and against any and all claims, suits and damages asserted by any third Person, and all related costs, fees and expenses (including reasonable attorneys' and experts' fees and court costs) suffered or incurred by any ROCHE Indemnitee arising out of, resulting from or otherwise concerning

(i) any breach by GPRO of its warranties set forth in Section 8.2, or (ii) the HPV TMA Test Kits, including, without limitation, the manufacture, use or sale of the HPV TMA Test Kits, except to the extent that any such claim, suit or damages asserted by any third Person arises out of, results from or otherwise concerns any breach of the warranties provided by ROCHE in Section 8.1.2 or 8.2. For the avoidance of doubt, GPRO's indemnity obligations under this Section 8.4.2 shall extend to all claims by any third Person(s) for infringement of any patent other than those included within the ROCHE HPV Patents.

8.4.3 A party indemnifying and holding an Indemnitee harmless under Section 8.4.1 or Section 8.4.2 above (an "Indemnitor") shall defend any such claim or suit asserted by the third Person and shall be entitled to control the defense and settlement thereof, provided that the Indemnitee may participate in such defense at its sole cost and expense and, provided, further, that the Indemnitee shall cooperate fully in such defense (such as by providing documents and giving testimony, as appropriate) as reasonably requested by the Indemnitor.

8.5 Limitation of Liability.

NOTWITHSTANDING ANY OTHER PROVISION OF THIS AGREEMENT, IN NO EVENT SHALL ROCHE OR GPRO BE LIABLE, WHETHER IN CONTRACT, TORT, WARRANTY, INDEMNITY OR UNDER ANY STATUTE OR ON ANY OTHER BASIS WHATSOEVER FOR SPECIAL, INCIDENTAL, INDIRECT, PUNITIVE, MULTIPLE OR CONSEQUENTIAL DAMAGES SUSTAINED BY THE OTHER PARTY OR ANY OTHER PERSON OR ENTITY ARISING OUT OF SUCH PARTY'S RESPECTIVE PERFORMANCE OR FAILURE TO PERFORM ITS OBLIGATIONS UNDER THIS AGREEMENT INCLUDING THOSE RELATING TO THE MANUFACTURE OR SALE OF HPV PRODUCTS OR HPV TMA TEST KITS OR THE PERFORMANCE OF SERVICES, OR THE POSSESSION OR USE OF ANY HPV PRODUCT OR HPV TMA TEST KITS, WHETHER OR NOT FORESEEABLE AND WHETHER OR NOT ROCHE OR GPRO, AS APPLICABLE, IS ADVISED OF THE POSSIBILITY OF SUCH DAMAGES, INCLUDING, WITHOUT LIMITATION, DAMAGES ARISING FROM OR RELATING TO LOSS OF USE, DOWNTIME, OR LOSS OF REVENUE, PROFITS, GOODWILL, OR BUSINESS OR OTHER FINANCIAL LOSS. **NOTHING CONTAINED IN THIS SECTION 8.5 SHALL LIMIT OR WAIVE A PARTY'S RIGHT TO SEEK SPECIFIC PERFORMANCE OF THIS AGREEMENT OR ANY REMEDY OTHER THAN SPECIAL, INCIDENTAL, INDIRECT, PUNITIVE, MULTIPLE OR CONSEQUENTIAL DAMAGES.**

9. Term and Termination.

9.1 Term. This Agreement shall become effective as of the Effective Date and shall continue in effect until the expiration of the last to expire of the ROCHE HPV Patents or unless terminated earlier in accordance with the terms and conditions of this Section 9. Upon any such termination, GPRO will have no further obligation to purchase the HPV Products from ROCHE and ROCHE will have no further obligation to manufacture and supply the HPV Products to GPRO.

9.2 Termination for Breach. Either party may terminate this Agreement at any time, in response to a material breach by the other party by giving the other party notice of such intention to terminate and sixty (60) Days to cure the material breach. If the other party fails to cure the material breach within such sixty (60) day period, such party may terminate this Agreement by further written notice of termination to the other party. Such termination shall not affect any other legal or equitable remedies for breach which the terminating party may have.

9.3 Other Termination Rights.

(i) ROCHE may terminate this Agreement by written notice to GPRO due to actual claims or actions brought or commenced against ROCHE by any third Person alleging that ROCHE's performance under this Agreement constitutes a breach of an existing agreement to which ROCHE is bound or subject or an infringement of such Person's intellectual property rights; *provided however*, that ROCHE may terminate this Agreement under this Section 9.3 only if (a) ROCHE has consulted with GPRO in good faith to discuss the subject claims or actions and potential responses thereto, and (b) ROCHE concludes, in the exercise of its commercially reasonable judgment (including consideration of all proposals made by GPRO in the course of the parties' good faith consultation), that failure to terminate this Agreement might (I) substantially prejudice ROCHE' rights under an existing agreement to which ROCHE is bound or subject, or (II) constitute an infringement of intellectual property rights of a third Person that are encompassed by an existing agreement to which ROCHE is bound or subject. Subject to the following restrictions and limitations, in the event of any such termination by ROCHE on or before December 31, 2012, ROCHE will pay GPRO the amount of the Manufacturing Access Fees paid by GPRO through the date of termination, less a dollar amount equal to (a) the product of (i) the number of Individual HPV Test Quantities sold by ROCHE to GPRO through the date of termination, and (ii) $0.75 per Individual HPV Test Quantity so sold, plus (b) the sum of (i) Three Million Dollars ($3,000,000), and (ii) an amount equal to fifty percent (50%) of ROCHE's attorneys' and experts' fees and costs suffered or incurred by ROCHE in the defense of such actual claims or actions (up to a maximum of US$2,000,000). If any such termination occurs on or after January 1, 2013, GPRO shall not be entitled to any Manufacturing Access Fees or other payment from ROCHE as a consequence of such termination.

(ii) Notwithstanding any other provision of this Agreement, Sections 8.4.1 and 9.3 set forth the entire liability of ROCHE in connection with any breach by ROCHE of the warranty provided in Section 8.1.2, the subject matter of this

Section 9.3 or any such termination, and constitute the sole remedy of GPRO in regard to any of the foregoing.

9.4 Termination in the Event of Bankruptcy. Either party shall have the right to terminate this Agreement effective immediately upon written notice to the other party if such other party (i) files in any court or agency pursuant to any bankruptcy or insolvency law a case or petition in bankruptcy or insolvency or for reorganization or similar arrangement or for the appointment of a receiver or trustee of such party or its assets, (ii) is served with an involuntary case or petition against it in any insolvency proceeding, which case or petition has not been stayed or dismissed within 60 days after service upon such party, or (iii) makes an assignment for the benefit of its creditors.

9.5 Effect of Termination. Upon the termination of this Agreement, except with regard to accepted purchase orders which shall remain in full force and effect and be performed by the parties in accordance with their respective terms and conditions, the respective obligations of the parties hereunder shall concurrently terminate, provided however, that the provisions of Sections 6.2, 6.3, 8, 11 and 12 shall survive and remain in full force and effect in accordance with their terms, conditions and limitations and all other provisions hereof which would reasonably be expected to survive termination shall so survive.

10. Alternative Manufacturing Site.

10.1 Alternative Manufacturing Site. ROCHE may manufacture the HPV Products at its manufacturing facilities in New Jersey, U.S.A. or in Germany, or at any ROCHE approved third-Person supplier manufacturing site (each an "Alternative Manufacturing Site"); provided, however, that GPRO shall not have the right, and ROCHE shall not grant to GPRO the right, to manufacture the HPV Products on ROCHE's behalf or otherwise. ROCHE agrees to qualify one Alternative Manufacturing Site, to be selected in ROCHE's sole discretion, as a secondary site for the manufacture of HPV Products for ROCHE for sale to GPRO hereunder. Upon commencement of manufacturing at any site other than ROCHE's manufacturing facilities in New Jersey, U.S.A., the parties shall reasonably agree upon a reasonable process to establish the equivalency, as determined by performance testing, of the HPV Products manufactured at such site to the HPV Products manufactured at the New Jersey facilities.

11. Confidentiality.

11.1 Confidentiality Obligations. Except as expressly authorized in writing, neither ROCHE nor GPRO shall disclose to any third Person or use any Confidential Information of the other party except as reasonably necessary to exercise its rights and perform its obligations hereunder. Neither ROCHE nor GPRO shall disclose any Confidential Information of the other party to any third Person that has not agreed in writing to keep such information confidential. Any reproduction or

copy of Confidential Information shall carry the same proprietary and/or confidential notices and legends that appear on the original. The parties agree that any breach of the restrictions contained in this Section 11.1 will cause irreparable harm to the non-breaching party, entitling such party to injunctive relief in addition to all other legal remedies.

11.2 Exceptions. The recipient of any Confidential Information of the other party shall be relieved of this obligation of confidentiality and restriction on use to the extent that: (i) such information was in the public domain at the time it was disclosed or has become in the public domain through no fault of the recipient; (ii) the recipient can prove such information was known to it, without restriction, at the time of disclosure as shown by the files of the recipient in existence at the time of disclosure; (iii) such information is disclosed by the recipient with the prior written approval of the other party; (iv) the recipient can prove such information was independently developed by it without any use of the other party's Confidential Information; (v) such information becomes known to the recipient, without restriction, from a source other than the other party without breach of this Agreement, or (vi) the recipient is required to disclose such Confidential Information by the rules of a securities exchange to which a party is subject, applicable law, regulation or order of a governmental agency or a court of competent jurisdiction, provided that the recipient shall provide written notice thereof to the other party and sufficient opportunity to object to any such disclosure or to request confidential treatment thereof.

12. General.

12.1 Force Majeure. Neither party shall be liable for any failure or delay in its performance, other than the payment of funds due under this Agreement, due to causes, including, but not limited to, acts of God, acts of civil or military authority, fires, epidemics, floods, earthquakes, riots, wars, sabotage, labor shortages or disputes, governmental actions or any other events, which are beyond its reasonable control. The delayed party shall: (i) give the other party written notice of such cause promptly, and in any event within fifteen (15) Days of discovery thereof, and (ii) use its reasonable efforts to correct such failure or delay in its performance. The delayed party's time for performance or cure under this Section shall be extended for a period equal to the duration of the cause.

12.2 Relationship of Parties. GPRO is an independent contractor. Neither GPRO nor GPRO's employees, consultants, contractors or agents are agents, fiduciaries, employees or joint venturers of ROCHE, nor do they have any authority to bind ROCHE by contract or otherwise to any obligation. They will not represent to the contrary, either expressly, implicitly, by appearance or otherwise.

12.3 Assignment. Neither GPRO nor ROCHE may assign or transfer (whether by merger, operation of law or in any other manner) any of its rights or delegate any of its obligations under this Agreement without the express prior written consent of the other party; provided that, without limitation of or breaching this Section

12.3: (i) a party may assign or transfer any of its rights or delegate any of its obligations under this Agreement, in whole or in part, to any of its Affiliates, without the consent of the other party, but without relieving the delegating party from the responsibility for performance of any of such obligations, and (ii) a party may assign or transfer its rights or delegate its duties and obligations (in whole and not in part) under this Agreement to any Person which acquires all, or substantially all, of its assets and/or business, provided that such assignee or transferee duly and effectively assumes all of the obligations of the assigning or transferring party hereby by an instrument reasonably satisfactory to the other party, and provided further, that in the case of GPRO's assignee or transferee, such assignee or transferee shall be approved in writing by ROCHE prior to such assignment or transfer, provided that ROCHE's approval shall not be unreasonably withheld. If ROCHE reasonably withholds consent as to any proposed assignee or transferee, then GPRO may validly effect such assignment or transfer by paying ROCHE (i) if the proposed assignment or transfer is to occur at anytime prior to January 1, 2015, the sum of US$10,000,000, and (ii) if the proposed assignment or transfer is to occur at anytime on or after January 1, 2015, the sum of US$5,000,000. Any assignment or transfer in violation of the provisions of this section shall be void and shall constitute a material breach of this Agreement. Subject to the foregoing, this Agreement shall be binding upon and shall inure to the benefit of each party's respective permitted successors and permitted assigns.

12.4 Rights of and Performance by Affiliates. To the extent that any term or provision of this Agreement grants rights to or contemplates, permits or requires performance by any Affiliate of a party, such Affiliate shall be considered to be an intended third party beneficiary of this Agreement, and such party shall cause such Affiliate to perform each and every obligation of such party under this Agreement in accordance with the terms and conditions hereof.

12.5 Applicable Law; Arbitration. This Agreement shall be governed by and construed in accordance with the laws of the State of California, excluding its conflict of laws principles. Any dispute, controversy or claim by or between ROCHE and GPRO arising out of or relating to this Agreement or the matters or transactions contemplated herein shall be settled by binding arbitration in San Francisco, California if initiated by GPRO and in San Diego, California if initiated by ROCHE, conducted in accordance with the Commercial Arbitration Rules of the American Arbitration Association, and judgment on any award rendered in any such arbitration may be entered in any court having jurisdiction over a party or its property.

12.6 Severability. If for any reason an arbitration panel finds any provision of this Agreement, or portion thereof, to be unenforceable, that provision of the Agreement shall be enforced to the maximum extent permissible so as to effect the intent of the parties, and the remainder of this Agreement shall continue in full force and effect.

12.7 No Waiver. Failure by either party to enforce any provision of this Agreement shall not be deemed a waiver of future enforcement of that or any other provision.

12.8 Complete Agreement. This Agreement, including all attachments and exhibits, constitutes the entire agreement between the parties with respect to the subject matter hereof, and supersedes and replaces all prior or contemporaneous understandings or agreements, written or oral, regarding such subject matter. No amendment to or modification of this Agreement shall be binding unless in writing and signed by a duly authorized representative of both parties.

12.9 Benefit; No Third Party Beneficiaries. Except as expressly contemplated herein, this Agreement is entered into solely for the benefit of the parties hereto, and the provisions of this Agreement will be for the sole and exclusive benefit of such parties. Except as expressly contemplated herein, nothing herein contained will be deemed to create any third party beneficiaries or confer any benefit or rights on or to any third Person, and no third Person will be entitled to enforce any provisions hereof or exercise any rights hereunder, except as expressly contemplated herein.

12.10 Headings; Sections and Exhibits. Headings contained in this Agreement are for convenience only and will not be used in the interpretation of this Agreement. References herein to sections, schedules and exhibits are to the sections, schedules and exhibits, respectively, of this Agreement. The schedules and exhibits are hereby incorporated herein by reference and made a part of this Agreement. Should any inconsistency exist or arise between a provision of this Agreement and a provision of any exhibit, schedule, or other incorporated writing, the provision of this Agreement will prevail.

12.11 No Construction Against Drafter. Each party and its counsel have participated fully in the review and preparation of this Agreement. Any rule of construction to the effect that ambiguities are to be resolved against the drafting party will not apply in interpreting this Agreement.

12.12 Certain Words and Terms. Unless the context clearly requires otherwise: (i) the plural and singular numbers will each be deemed to include the other; (ii) "shall", "will," "will agree," or "agrees" are mandatory, and "may" is permissive; (iii) "or" is not exclusive; and (iv) "includes" and "including" are not limiting.

12.13 Counterparts. This Agreement may be executed in any number of counterparts, and each counterpart will be deemed an original instrument, but all counterparts together will constitute but one agreement.

12.14 Notices. All notices, requests, demands, or other communications under this Agreement will be in writing. Notice will be sufficiently given for all purposes as follows: (i) when personally delivered to the recipient, notice is effective on

delivery; (ii) when mailed certified mail, return receipt requested, notice is effective on receipt, if delivery is confirmed by a return receipt; (iii) when delivered by Federal Express/Airborne/United Parcel Service/DHL WorldWide, or United States Express Mail, charges prepaid or charged to the sender's account, notice is effective on delivery, if delivery is confirmed by the delivery service; and (iv) when sent by fax to the last fax number of the recipient known to the party giving notice, notice is effective on receipt, provided that: (a) a duplicate copy of the notice is promptly given by first-class or certified mail or by overnight delivery, or (b) the receiving party delivers a written confirmation of receipt. Any notice given by fax will be deemed received on the next business day if it is received after 5:00 p.m. (recipient's time) or on a non-business day.

12.15 Notice Refused, Unclaimed, Or Undeliverable. Any correctly addressed notice that is refused, unclaimed, or undeliverable because of an act or omission of the party to be notified will be deemed effective as of the first date that said notice was refused, unclaimed, or deemed undeliverable by the postal authorities, messenger, or overnight delivery service.

12.16 Addresses. Addresses for purpose of giving notice are as set forth immediately below, or such other addresses as may be designated in writing by the parties from time to time during the term of this Agreement:

If to ROCHE: Roche Molecular Systems, Inc.
4300 Hacienda Drive
Pleasanton, CA 94588
FAX No.: (510) 814-2956
Attn.: General Counsel

If to GPRO: Gen-Probe Incorporated
10210 Genetic Center Drive
San Diego, CA 92121
FAX No.: 858-410-8637
Attn.: General Counsel

12.17 Publicity and Confidentiality of Agreement. Each party and its Affiliates shall maintain the confidentiality of all provisions of this Agreement and neither party nor any of its Affiliates shall make any public announcement of or otherwise disclose to any third Person this Agreement or any of its terms without the prior written consent of the other party, except that a party may disclose such information as may have entered into the public domain through no fault of such party or as required by the rules of a securities exchange to which a party is subject or any applicable law or regulation based upon the written advice of counsel and then only with prior notice to the other party as far in advance as reasonably possible and with reasonable consideration to the advice of the other

party as to how such disclosure could be modified to conform with applicable rules, laws and regulations and still protect the confidentiality interests of the other party. The parties further agree that in the event that either party wishes to prepare and publicly disseminate a press release announcing the product purchase and supply relationship provided herein, such party shall provide the other party a written draft of such release at least seven (7) days prior to the intended date of release, and the other party shall have the right to make reasonable modifications to such draft press release during such seven (7) day review period.

IN WITNESS WHEREOF, the parties hereto have duly executed this Agreement to be effective as of the Effective Date.

ROCHE MOLECULAR SYSTEMS, INC.	GEN-PROBE INCORPORATED
By:_____	By:_____
_____ Printed Name	Henry L. Nordhoff
_____ Title	President and Chief Executive Officer Title
Date:_____	Date: _____
By:_____	
_____ Printed Name	
_____ Title	
Date:_____	

(Signatures Continued on Next Page)

F. HOFFMANN-LA ROCHE LTD.

By:_____

_____
Printed Name

_____
Title

Date:_____

By:_____

_____
Printed Name

_____
Title

Date:_____

EXHIBIT A

ROCHE HPV PATENTS

EXHIBIT A

LICENSED ROCHE HPV PATENTS

The following patents and patent applications are included within the scope of the April 1, 1990 Cross License Agreement originally entered into between Life Technologies, Inc. and Institut Pasteur and are subject to the terms, conditions, restrictions and limitations therein. ROCHE represents and warrants that, as of the Effective Date, it is the assignee by written agreement to the rights of Institut Pasteur under the said Cross License Agreement.

United States Patent Application:

Application for HPV 31	No. US 053776	Applic	870319

Issued United States Patents:

Patent for HPV 35	No. US 4849332	Applic Issued	870526 890718
Patent for HPV 43	No. US 4849334	Applic Issued	870609 890718
Patent for HPV 56 (formerly HPV 57)	No. US 4908306	Applic Issued	870612 900313

Other Patent Applications (All Types Except HPV 31; U.S. priority)

Canadian	No. 567658
Japanese	No. 129427/88
European	No. 88108418.0

OWNED ROCHE HPV PATENTS

The patents and patent applications listed on Attachment "1" to this Exhibit "A" were originally owned by Institut Pasteur or co-owned by Institut Pasteur and Centre National de la Recherche Scientifique ("CNRS"). ROCHE represents and warrants that, as of the Effective Date, it is the successor-in-interest, by written assignment, to the rights of Institut Pasteur and CNRS therein.

***Confidential Treatment Requested

GPRO acknowledges that Roche has informed GPRO that U.S. patent no. 5,981,173 and its foreign counterparts were acquired by Roche from Institut Pasteur subject to an exclusive license in favor of Digene Corporation. Until such time as the said exclusive license terminates or expires, Roche's rights in this U.S. patent and its foreign counterparts are subject to the terms, conditions, limitations and restrictions of the said exclusive license.

INTERNALLY DEVELOPED/OWNED ROCHE HPV PATENTS

U.S. Patent No. 5,527,898 – directed to various HPV probes and primers

U.S. Patent No. 5,639,871 – directed to various HPV probes

U.S. Patent No. 5,182,377 – directed to various HPV probes

U.S. Patent No. 5,447,839 – directed to methods of detecting HPV using various HPV probes

U.S. Patent No. 5,705,627 – directed to various HPV probes

U.S. Patent No. 5,283,171 – directed to methods of detecting HPV using amplification with certain HPV primers and to various HPV oligonucleotides

Pending ROCHE HPV-Related Patent Applications:

U.S. Provisional Patent Application Serial No. 60/568,934 (filed May 7, 2004) – "High-Risk Human Papilloma Virus Detection" – directed to various HPV-related oligonucleotides including ROCHE's cross-reactive probes.

Attachment 1 to Exhibit A
To Supply and Purchase Agreement

Owned Roche Patents

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Determined DNA sequences derived from a papillomavirus genome, their uses for in vitro diagnostic purposes and the production of antigenic compositions

Ep-Dossier 220381 EP 01 SEQUENCES DE L'HPV 33 Inventeur: COLLET CHLE STEGMAT
N° D.I 185831 SEQUENCES DE L'HPV 33

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3	N° Délivrance	Date
220381 AT 02	AUTRICHE	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 AU 01	AUSTRALIE	AU7200787	20/03/1987		INSTITUT PASTEUR			615159	26/09/1991
220381 BE 02	BELGIQUE	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 CA 01	CANADA	CA532925	25/03/1987		INSTITUT PASTEUR			1341100	26/09/2000
220381 CA 02	CANADA	CA617043	25/03/1987	Division	INSTITUT PASTEUR			1341339	25/12/2001
220381 CH 02	SUISSE	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 DE 02	ALLEMAGNE	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 DK 01	DANEMARK	DK488987	20/03/1987		INSTITUT PASTEUR				
220381 EP 02	BEP.EUROP.	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 ES 01	ESPAGNE	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 FI 01	FINLANDE	FI875662	20/03/1987		INSTITUT PASTEUR			100857	15/09/1997
220381 FR 02	FRANCE	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 GB 02	GR.BRETAG.	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 GR 01	GRECE	EU874006356	20/03/1987		INSTITUT PASTEUR			GR1006272/0243221	20/05/1992
220381 IT 02	ITALIE	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 JP 01	JAPON	JP62196887	20/03/1987		INSTITUT PASTEUR			2633275	25/04/1997
220381 JP 02	JAPON	JP27382496	20/03/1987	Division	INSTITUT PASTEUR			2735537	9/01/1998
220381 KR 01	COREE SUD	KR8701075	20/03/1987		INSTITUT PASTEUR			69843	13/01/1994
220381 LI 02	LIECHTENST	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 LU 02	LUXEMBOURG	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 NL 02	PAYS-BAS	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 NO 01	NORVEGE	NO874758	20/03/1987		INSTITUT PASTEUR			303287	22/06/1998
220381 SE 02	SUEDE	EU874006356	20/03/1987		INSTITUT PASTEUR			0243221	20/05/1992
220381 US 06	ETATS-UNIS	US5221349	24/03/1994	Contin° in Part	INSTITUT PASTEUR			5554538	10/09/1996
220381 US 09	ETATS-UNIS	US6666711	6/06/1995	Division	INSTITUT PASTEUR			5648439	15/07/1997
220381 US 11	ETATS-UNIS	US891801	15/07/1997	Division	INSTITUT PASTEUR			5876723	2/03/1999
220381 US 13	ETATS-UNIS	US338076	11/06/1999	Continuation	INSTITUT PASTEUR			6107086	25/05/2000
220381 US 13	ETATS-UNIS	US877693	25/05/2000	Continuation	INSTITUT PASTEUR			6242250	5/06/2001
220381 US 14	ETATS-UNIS	US633969	12/04/2001	Continuation	INSTITUT PASTEUR			6746314	5/02/2002
220381 US 15	ETATS-UNIS	US n° en attente	19/12/2001	Continuation	INSTITUT PASTEUR				

* Confidential
Treatment Requested

(11) Publication number: **0 243 221 B1**

(12) # EUROPEAN PATENT SPECIFICATION

(15) Date of publication of patent specification: 20.05.92

(51) Int. Cl[5]: **C12N 15/37**, A61K 39/12, A61K 39/42, C12Q 1/70

(21) Application number: 87400635.6

(22) Date of filing: 20.03.87

(54) Determined DNA sequences derived from a papillomavirus genome, their uses for In vitro diagnostic purposes and the production of antigenic compositions.

(30)Priority: 21.03.86 EP 86400609

(43) Date of publication of application:
28.10.87 Bulletin 87/44

(45) Publication of the grant of the patent:
20.05.92 Bulletin 92/21

(64) Designated Contracting States:
AT BE CH DE ES FR GB GR IT LI LU NL SE

(58) References cited:
EP-A- 0 192 001
WO-A-87/01375

UCLA SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, PAPILLOMAVIRUSES: MOLECULAR AND CLINICAL ASPECTS, vol. 32, 1985, pages 391-396, Alan R. Liss, Inc.,; K. SEEDORF et al.: "Human papillomavirus type 16 DNA: Expression of open reading frames In E. coll"

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(74) Representative: Gutmann, Ernest et al
S.C. Ernest Gutmann - Yves Plasseraud 67 boulevard Haussmann
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ADN SEQUENCES OF THE HUMAN PAPILLOMAVIRUS TYPE 42, AND DIAGNOSTIC APPLICATION THEREOF

Se-Dossier 250016 FR 01 HPV 42 — Inventeur: COLLEU COLE SIMONET

N° D.I 191012 SEQUENCE DE L'HPV 42

N° Se-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1 Co-Propriétaire 2 Co-Propriétaire 3	N° Délivrance	Date
------- -- --	FRANCE	EP9108125	28/06/1991		INSTITUT PASTEUR	9108125	8/10/1993
250016 AT 01	AUTRICHE	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 AU 01	AUSTRALIE	AU71746392	25/06/1992		INSTITUT PASTEUR	673498	4/03/1997
250016 BE 01	BELGIQUE	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 CA 01	CANADA	CA2112896	25/06/1992		INSTITUT PASTEUR		
250016 CH 01	SUISSE	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 DE 01	ALLEMAGNE	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 DK 01	DANEMARK	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 EP 01	DEP.EUROP.	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 ES 01	ESPAGNE	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 FR 02	FRANCE	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 GB 01	GB,ROYAUM.	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 GR 01	GRECE	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 IT 01	ITALIE	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 LI 01	LIECHTENST	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 LU 01	LUXEMBOURG	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 MC 01	MONACO	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 NL 01	PAYS-BAS	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 SE 01	SUEDE	EU9229139756	25/06/1992		INSTITUT PASTEUR	0591376	31/03/1998
250016 US 01	ETATS-UNIS	US5167856	25/06/1992		INSTITUT PASTEUR	5952487	14/09/1999

1-3

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(11) Publication No: **2 678 284**
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(21) National file no.: **91 08125**

(51) Int. Cl.[6]: C12N 15/37, C1Q 1/68

(12) **PATENT** **B1**

(54) DNA SEQUENCES DERIVED FROM THE GENOME OF PAPILLOMAVIRUS HPV42, APPLICATION OF THESE SEQUENCES FOR THE IN VITRO DIAGNOSIS OF INFECTIONS BY THE PAPILLOMAVIRUS AND FOR THE PRODUCTION OF IMMUNOGENIC COMPOSITIONS.

(22) Filing date: 6/28/91.

(30) Priority:

(43) Publication date of the application: 12/31/92 Bulletin 92/53.

(45) Publication date of the patent: 10/8/93 Bulletin 93/40.

(56) List of documents cited in the search report:

Refer to the end of this publication

(60) References to other related national documents:

(71) Applicant(s): PASTEUR INSTITUTE PRIVATE FOUNDATION RECOGNIZED BY THE PUBLIC UTILITY – FR

(72) Inventor(s): PHILIPP WOLFGANG - DR. SAPP MARTIN - DR. COLE STEWART AND HONORE NADINE

(73) Owner(s):

(74) Agent(s): GUTMANN ERNEST - PLASSERAUD YVES S.A.

Papilloma virus probes and in vitro methods for the diagnosis of Papilloma virus infections.

Ss-Dossier 213623 FR 04 SONDE A PAPILLOMAVIRUS III Inventeur: OKIMOTO CHRISTIAN
N° D.I 103036 SONDES PAPILLOMAVIRUS

N° Ss-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3	N° Délivrance	Date
213623	FR 01 FRANCE	EP8601623	31/01/1986	Addition	CNRS	INSERM	INSTITUT PASTEUR	8601625	4/05/1990
213623	AT 01 AUTRICHE	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	891157	30/06/1993
213623	BE 01 BELGIQUE	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	0235004	30/06/1993
213623	CA 01 CANADA	CA329178	6/02/1987		INSERM	INSTITUT PASTEUR	CNRS	1340691	8/02/2000
213623	CH 01 SUISSE	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	0235004	30/06/1993
213623	DE 01 ALLEMAGNE	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	P37863576	30/06/1993
213623	DK 01 DANEMARK	DK32987	2/02/1987		INSTITUT PASTEUR	CNRS	INSERM		
213623	ES 01 ESP.,EUROP.	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS		
213623	ES 01 ESPAGNE	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	0235004	30/06/1993
213623	FI 01 FINLANDE	FI870366	30/01/1987		INSTITUT PASTEUR	CNRS	INSERM	100487	28/11/1997
213623	FR 05 FRANCE	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	0235004	30/06/1993
213623	GB 01 GR.BRETAG.	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	0235004	30/06/1993
213623	GR 01 GRECE	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	0235004	30/06/1993
213623	IT 01 ITALIE	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	0235004	30/06/1993
213623	JP 01 JAPON	JP8303404687	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	2716120	7/11/1997
213623	LI 01 LIECHTENST	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS		
213623	LU 01 LUXEMBOURG	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	0235004	30/06/1993
213623	NL 01 PAYS-BAS	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	0235004	30/06/1993
213623	SE 01 SUEDE	EU874002181	30/01/1987		INSERM	INSTITUT PASTEUR	CNRS	0235004	30/06/1993
213623	TW 01 TAIWAN	TW76101801	3/04/1987		INSTITUT PASTEUR	CNRS	INSERM	130889	2/08/1989
213623	US 14 ETATS-UNIS	US914005	16/07/1992	Contin° :	INSERM	INSTITUT PASTEUR	CNRS	5411057	2/05/1995
213623	US 17 ETATS-UNIS	US415511	3/06/1995	Division	INSERM	INSTITUT PASTEUR	CNRS	5665671	9/09/1997
213623	US 18 ETATS-UNIS	US479145	7/06/1995	Continuation	INSERM	INSTITUT PASTEUR	CNRS	5958674	28/09/1999
213623	US 13 ETATS-UNIS	US876159	16/07/1996	Contin°	INSERM	INSTITUT PASTEUR	CNRS	5712092	27/01/1998
213623	US 16 ETATS-UNIS	US483168	7/06/1995	Continuation	INSERM	INSTITUT PASTEUR	CNRS	5876923	2/03/1999
213623	US 20 ETATS-UNIS	US934659	22/09/1997	Division	INSERM	INSTITUT PASTEUR	CNRS		
213623	US 21 ETATS-UNIS	US987557	15/11/2001	Division	INSERM	INSTITUT PASTEUR	CNRS		

(11) Publication number: **0 235 004 B1**

(12) # EUROPEAN PATENT SPECIFICATION

(45) Publication date of the paten specification: 6/30/93

(51) Int. Cl[5]: **C12Q 1/70**, C12N 15/00

(31) File number: 8740021.1

(33) Filing date: 1/30/87

(54) Papillomavirus tests with and method of in vitro diagnosis of papillomavirus infections

(30) Priority: 1/31/86 FR 8601425

(43) Publication date of the application:
9/2/87 Bulletin 87/36

(45) Notice of the patent grant:
6/30/93 Bulletin 93/26

(54) Designated contracting states:
AT BE CH DE ES FR GB GR IT LI LU NL SE

(56) Documents cited:
EP-A- 0 192 001

JOURNAL OF VIROLOGY, vol. 52, No 3, December 1984, American Society for Microbiology (US); D. KREMSDORF et al., pp. 1013-1018

CHEMICAL ABSTRACTS, vol. 108, No 7, February 1988, Columbus, OH (US); S. BEAUDENON and al., p. 396, No 52535w

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CODING DNA FRAGMENTS FOR POLYPEPTIDES CONTAINING AT LEAST ONE ANTIGENIC DETERMINANT OF THE PAPILLOMAVIRUS PARTICULARLY OF THE Ia HPV TYPE AND CORRESPONDING POLYPEPTIDES

Se-Dossier 205531 FR 01 PAPILLOMAVIRUS Inventeur: DARDEL DANOS OLIVIER
N° D.I 182011 PAPILLOMAVIRUS

N° Se-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3	N° Délivrance	Date
205531 BE 01	BELGIQUE	BE0139010816	1/04/1983		INSTITUT PASTEUR	CNRS		0104217	14/09/1988
205531 CA 01	CANADA	CA425145	5/04/1983		INSTITUT PASTEUR	CNRS		1199595	21/01/1986
205531 CH 01	SUISSE	EP0139010816	1/04/1983		INSTITUT PASTEUR	CNRS		0104217	14/09/1988
205531 DE 01	ALLEMAGNE	EP0139010816	1/04/1983		INSTITUT PASTEUR	CNRS		33779899/0104217	14/09/1988
205531 EP 01	BRP.EUROP.	EP0146006092	1/04/1983		INSTITUT PASTEUR	CNRS		0092456	17/08/1988
205531 EP 02	BRP.EUROP.	EP0139010816	1/04/1983		INSTITUT PASTEUR	CNRS		0104217	14/09/1988
205531 GB 01	GR.BRETAG.	EP0139010816	1/04/1983		INSTITUT PASTEUR	CNRS		0104217	14/09/1988
205531 IT 01	ITALIE	EP0146006092	1/04/1983		INSTITUT PASTEUR	CNRS		0092456	17/08/1988
205531 JP 01	JAPON	JP58117883	1/04/1983		INSTITUT PASTEUR	CNRS		2677548	25/07/1997
205531 JP 02	JAPON	JP13397196	1/04/1983	Division	INSTITUT PASTEUR	CNRS		2768938	10/04/1998
205531 LI 01	LIECHTENST	EP0139010816	1/04/1983		INSTITUT PASTEUR	CNRS		0104217	14/09/1988
205531 NL 01	PAYS-BAS	EP0139010816	1/04/1983		INSTITUT PASTEUR	CNRS		0104217	14/09/1988
205531 US 01	ETATS-UNIS	US538168	1/04/1983		INSTITUT PASTEUR	CNRS		4551276	5/11/1985

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(11) Publication No: **2 524 487**
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(21) National file no.: **82 05887**

(51) Int. Cl.^{3}: C12N 15/00; A81K 39/385; G01N 33/50.

(12) **PATENT** **B1**

(54) DNA fragments that code for polypeptides containing at least one antigenic determinant of the papillomavirus, in particular of type HPV 1a and the corresponding polypeptides.

(22) Filing date: April 5, 1982

(30) Priority:

(43) Publication date of the application:
BOPI "Patents" no. 40 of October 7, 1983.

(45) Publication date of the patent:
BOPI "Patents" no. 47 of November 22, 1985.

(56) List of documents cited in the search report:

Refer to the end of this publication

(60) References to other related national documents:

(71) Applicant(s): PASTEUR INSTITUTE - FR

(72) Inventor(s): Olivier Danos. Michaël Katinka and Moshe Yaniv.

(73) Owner(s):

(74) Agent(s): Cabinet Plasseraud.

Papilloma virus probes and in vitro methods for the diagnosis of papilloma virus infections

Sa-Dossier 213631 FR 03 SONDE A PAPILLOMAVIRUS Inventeur: CHIH GERARD

N° Sa-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3	N° Délivrance	Date
-------	-- --	FRANCE	BF8418369	30/11/1984	CNRS	INSERM	INSTITUT PASTEUR	8418369	9/11/1987
213621	AT 01	AUTRICHE	EU0540236291	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	873501	11/03/1992
213621	BE 01	BELGIQUE	EU0540236291	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	0192001	11/03/1992
213621	CA 01	CANADA	CA496476	28/11/1985	INSERM	INSTITUT PASTEUR	CNRS	1276575	30/11/1990
213621	CH 01	SUISSE	EU0540236291	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	0192001	11/03/1992
213621	DE 01	ALLEMAGNE	EU0540236291	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	35856130	11/03/1992
213621	EP 01	DEP.EUROP.	EU0540236291	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	0192001	11/03/1992
213621	FR 03	FRANCE	EU0540236291	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	0192001	11/03/1992
213621	GB 01	GR.BRETAG.	EU0540236291	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	0192001	11/03/1992
213621	IT 01	ITALIE	EU0540236291	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	0192001	11/03/1992
213621	JP 01	JAPON	JP26522185	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	26522185	30/01/1990
213621	JP 03	JAPON	JP2265897	28/11/1985 Division	INSERM	INSTITUT PASTEUR	CNRS	2791322	12/06/1998
213621	LI 01	LIECHTENST	EU0540236291	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	0192001	11/03/1992
213621	LU 01	LUXEMBOURG	EU0540236291	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	0192001	11/03/1992
213621	NL 01	PAYS-BAS	EU0540236291	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	0192001	11/03/1992
213621	SE 01	SUEDE	EU0540236291	29/11/1985	INSERM	INSTITUT PASTEUR	CNRS	0192001	11/03/1992

Sa-Dossier 213629 FR 03 SONDE A PAPILLOMAVIRUS XI Inventeur: CHIH GERARD

N° Sa-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3	N° Délivrance	Date
-------	-- --	FRANCE	BF8507073	9/05/1985 Addition	CNRS	INSERM	INSTITUT PASTEUR	8507073	26/11/1986

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(11) Publication Number : 2 578 267
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(21) National file no.: 84 18369

(51) Int. Cl.[4]: C 12 N 15/00; C 12 P 10/34; C 12 Q 1/70; G 01 NR 33/569 / (C 12 Q 1/70, C 12 R 1:91).

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Paragraph 3a of article 57 of the decree 79 822 of 9/9/1979

(12) **PATENT** **B1**

(54) Papillomavirus tests and method of in vitro diagnosis of papillomavirus infections.

(22) Filing date: November 30, 1984.

(30) Priority:

(43) Publication date of the application:
BOPI "Patents" No. 36 of September 5, 1986.

(45) Publication date of the patent:
BOPI "Patents" No 47 of November 20, 1987.

(56) List of documents cited in the search report:

Refer to the end of this publication

(60) References to other related national documents:

(71) Applicant(s): *PASTEUR INSTITUTE, NATIONAL CENTER FOR SCIENTIFIC RESEARCH and NATIONAL INSTITUTE OF HEALTH AND MEDICAL RESEARCH, publicly-owned establishments* - FR

72) Inventor(s): Gerard Orth. Michel Fevre, Dina Kremsrdorf, Odile Croissant and Girard Pahau-Amaudet

(73) Owner(s):

(74) Agent(s): Cabinet Plasseraud.

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(11) Publication Number : **2 581 655**
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(21) National file no.: **85 07073**

(51) Int. Cl.[4]: C 12 Q 1/88; C 07 H 21/04; C 12 N 7/00, 15/00.

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Paragraph 3a of article 57 of the decree 79 822 of 9/9/1979

(12) **CERTIFICATE OF ADDITION TO A PATENT** **B2**

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(54) Papillomavirus tests and method of in vitro diagnosis of papillomavirus infections.

(22) Filing date: May 9, 1985.

(30) Priority:

(43) Publication date of the application:
BOPI "Patents" no. 48 of November 14, 1986.

(45) Publication date of the patent:
BOPI "Patents" no. 49 of December 9, 1988.

(56) List of documents cited in the search report:

Refer to the end of this publication

(60) References to other related national documents: Addition to the patent 84 18369 of November 30, 1984.

(71) Applicant(s): PASTEUR INSTITUTE, publicly-owned establishment; NATIONAL CENTER FOR SCIENTIFIC RESEARCH, publicly-owned establishment and NATIONAL INSTITUTE OF HEALTH AND MEDICAL RESEARCH, publicly-owned establishment – FR.

72) Inventor(s): Gerard Orth; Sylvie Beaudenon; Michel Favre; Odile Growing;l Dina Kremsdorf.

(73) Owner(s):

(74) Agent(s): S. C. Ernest Gutmann. Yves Plasseraud.

POLYPEPTIDES AND ANTIBODIES CHARACTERISTIC OF THE PAPILLOMAVIRUS, METHODS OF DIAGNOSIS AND VACCINES IN WHICH THEY ARE USED.

Co-Dossier 218541 FR 01 POLYPEPTIDES AND ANTIBODIES CHARACTERISTIC OF PAPILLOMAVIRUS Inventeur: CROWET CHOLLEBERT GEVILE

N° Co-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3	N° Délivrance	Date
------- -- --	FRANCE	EP8512750	26/08/1985		INSTITUT PASTEUR	INSTITUT PASTEUR		8512750	14/11/1988
218541 AT 01	AUTRICHE	EU8690468512	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		870288	11/12/1991
218541 BE 01	BELGIQUE	EU8690468512	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		0235187	11/12/1991
218541 CA 01	CANADA	CA516861	26/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		1279276	22/01/1991
218541 CH 01	SUISSE	EU8690468512	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		0235187	11/12/1991
218541 DE 01	ALLEMAGNE	EU8690468512	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		P3680893 /0235187	11/12/1991
218541 DK 01	DANEMARK	DK286987	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		173647	6/04/1999
218541 ES 01	ESP.EUROP.	EU8690468512	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		0235187	25/06/1991
218541 HU 01	HONGRIE	P3686011326	29/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		8601326	23/09/1988
218541 FR 02	FRANCE	EU8690468512	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		0235187	11/12/1991
218541 GB 01	GR.BRETAG.	EU8690468512	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		0235187	11/12/1991
218541 GR 01	GRECE	GR862201	26/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		862201	23/12/1986
218541 IT 01	ITALIE	EU8690468512	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		0235187	11/12/1991
218541 JP 01	JAPON	JP5844686	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		2759574	6/03/1998
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218541 LI 01	LIECHTENST	EU8690468512	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		0235187	11/12/1991
218541 LU 01	LUXEMBOURG	EU8690468512	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		0235187	11/12/1991
218541 NL 01	PAYS-BAS	EU8690468512	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		0235187	11/12/1991
218541 PT 01	PORTUGAL	PT83233	26/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		83233	3/01/1989
218541 SE 01	SUEDE	EU8690468512	22/08/1986		INSTITUT PASTEUR	INSTITUT PASTEUR		0235187	11/12/1991
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218541 US 10	ETATS-UNIS	US470471	6/06/1995	Division	INSTITUT PASTEUR	INSTITUT PASTEUR			

(11) Publication number: **0 235 187 B1**

(12) # EUROPEAN PATENT SPECIFICATION

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(86) International file number: PCT/FR86/00288

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WO 87/01375 3/12/87 Gazette 87/06

(51) Int. Cl.[5]: **C07K 15/00**, A61K 39/12, C12P 21/00, A61K 39/42, G01N 33/569, C12N 15/00, C 2N 15/37

(54) POLYPEPTIDES AND ANTIBODIES THAT ARE CARACTERISTIC OF THE PAPILLOMAVIRUS, METHODS OF DIAGNOSIS AND VACCINES USING THEM.

(30) Priority: 8/26/85 FR 8512750

(43) Publication date of the application:
9/8/87 Bulletin 87/37

(45) Date of notice of the patent grant:
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(54) Designated contracting states:
AT BE CH DE FR GB IT LI LU NL SE

(56) Documents cited:
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EP-A- 0 133 123
EP-A- 0 192 001
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*

Papillomavirus probes (HPV49, HPV50, HPV54, HPV55), products genetically and immunologically related to this papillomavirus and in vitro methods for the diagnosis of papillomavirus infections and for the production of antibodies against these papillomaviruses.

Sa-Dossier 230751 FR 02 PAPILLOMAVIRUS HPV49 50 54 55 Inventeur: CHITOU CHTH GERARD
N° D.I 188918 HPV-49, 50, 54, 55

N° Sa-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3	N° Délivrance	Date
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230751	FR 03	FRANCE	EU8940134424	12/05/1989		INSTITUT PASTEUR		0342128	26/04/1995
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230751	NL 01	PAYS-BAS	EU8940134424	12/05/1989		INSTITUT PASTEUR		0342128	26/04/1995
230751	SE 01	SUEDE	EU8940134424	12/05/1989		INSTITUT PASTEUR		0342128	26/04/1995
230751	US 02	ETATS-UNIS	US951110	25/09/1992 Continuation		INSTITUT PASTEUR		5342930	30/08/1994
230751	US 04	ETATS-UNIS	US2404F7	10/03/1994 Division		INSTITUT PASTEUR		5534439	9/07/1996
230751	US 05	ETATS-UNIS	US466381	6/06/1995 Division		INSTITUT PASTEUR		5593574	7/01/1997
230751	US 06	ETATS-UNIS	US426347	2/04/1990 Division		INSTITUT PASTEUR		5824456	20/10/1998
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Sa-Dossier 230752 FR 03 PAPILLOMAVIRUS HPV49 50 54 55B Inventeur: CHITOU CHTH GERARD

N° Sa-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3	N° Délivrance	Date
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Treatment Requested

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(11) Publication No: **2 631 341**
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(21) National file no.: **88 06486**

(51) Int. Cl.[4]: C 07 H 21/04; C 07 K 15/04; A 61 K 39/42; C 12 Q 1/68; G 01 N 33/53.

(12) **PATENT** **B1**

(54) TESTS FOR PAPILLOMAVIRUS HPV49, HPV50, HPV54, HPV55 AND PRODUCTS THAT ARE GENETICALLY AND IMMUNOLOGICALLY RELATED TO THESE PAPILLOMAVIRUSES HPV49, HPV50, HPV54, HPV55 AND METHOD OF IN VITRO DIAGNOSIS OF PAPILLOMAVIRUS INFECTIONS AND IN VIVO IMMUNIZATION AGAINST THESE PAPILLOMAVIRUSES

(22) Filing date: 5/13/88.

(30) Priority:

(43) Publication date of the application: 11/17/89 Bulletin 89/46

(45) Publication date of the patent: 4/26/91 Bulletin 91/17.

(56) List of documents cited in the search report:

Refer to the end of this publication

(60) References to other related national documents:

(71) Applicant(s): PASTEUR INSTITUTE, PRIVATE FOUNDATION RECOGNIZED PUBLIC UTILITY. - FR

(72) Inventor(s): GERALD ORTH - MICHEL FAVRE - DINA KREMSDORF - GERALD PEHAU-ARNAUDET

(73) Owner(s):

(74) Agent(s): S.C. ERNEST GUTMANN - YVES PLASSERAUD

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(21) National file no.: **88 08324**

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(12) **CERTIFICATE OF ADDITION TO A PATENT** **B2**

(54) TESTS FOR PAPILLOMAVIRUS HPV49, HPV50, HPV54, HPV55; PRODUCTS THAT ARE GENETICALLY AND IMMUNOLOGICALLY RELATED TO THESE PAPILLOMAVIRUSES HPV49, HPV50, HPV54, HPV55; METHOD OF IN VITRO DIAGNOSIS OF PAPILLOMAVIRUS INFECTIONS AND IN VIVO IMMUNIZATION AGAINST THESE PAPILLOMAVIRUSES

(22) Filing date: 6/21/88.

(30) Priority:

(43) Publication date of the application: 12/22/89 Bulletin 89/51.

(45) Publication date of the patent: 7/12/91 Bulletin 91/28.

(56) List of documents cited in the search report:

Refer to the end of this publication

(60) References to other related national documents: Addition to the patent 88 06486 of 5/13/88.

(71) Applicant(s): PASTEUR INSTITUTE PRIVATE FOUNDATION RECOGNIZED AS A PUBLIC UTILITY - FR

72) Inventor(s): GERALD ORTH - MICHEL FAVRE - DINA KREMSDORF - GERALD PEHAU-ARNAUDET.

(73) Owner(s):

(74) Agent(s): S. C. ERNEST GUTMANN - YVES PLASSERAUD.

1-17

HPV39 PAPILLOMAVIRUS GENOME-DERIVED DNA SEQUENCES, THEIR APPLICATION TO IN VITRO DIAGNOSIS AND PRODUCTION OF IMMUNOGENIC COMPOSITIONS.

* Confidential Treatment Requested

Su-Dossier 250026 FR 01 SEQUENCES DE L'HPV 39 Inventeur: CHIRAL CHIK GHANNO
N° D.I 198023 SEQUENCES DE L'HPV 39

N° Su-Dossier	Pays	N° Dépot	Date Dépot	Type de lien	Co-Propriétaire 1	Co-Propriétaire 2	Co-Propriétaire 3	N° Délivrance	Date
..... -- --	FRANCE	DF9016044	20/12/1990		INSERM	INSTITUT PASTEUR		9016044	19/08/1994
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250026 CH 01	SUISSE	EU929030344	20/12/1991		INSERM	INSTITUT PASTEUR		0563255	28/09/1994
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250026 NL 01	PAYS-BAS	EU929030344	20/12/1991		INSERM	INSTITUT PASTEUR		0563255	28/09/1994
250026 SE 01	SUEDE	EU929030344	20/12/1991		INSERM	INSTITUT PASTEUR		0563255	28/09/1994
250026 US 01	ETATS-UNIS	US5674879	20/12/1991		INSERM	INSTITUT PASTEUR		5634423	12/08/1997
250026 US 02	ETATS-UNIS	US5468857	6/06/1995	Division	INSERM	INSTITUT PASTEUR		5663535	9/09/1997

(11) Publication No: 2 670 797
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(21) National file no.: 90 16044

(51) Int. Cl.[6]: C 12 N 15/37, C 12 Q 1/68, C 07 K 15/28, G 01 N 33/567.

(12) **PATENT** **B1**

(54) DETERMINED DNA SEQUENCES DERIVED FROM THE GENOME OF PAPILLOMAVIRUS HPV39, APPLICATION OF THESE SEQUENCES FOR IN VITRO DIAGNOSIS OF INFECTION BY THIS PAPILLOMAVIRUS AND PRODUCTION OF AN IMMUNOGENIC COMPOSITION

(22) Filing date: 12/20/90.

(30) Priority:

(43) Publication date of the application: 8/28/92 Bulletin 92/26.

(45) Publication date of the patent: 8/19/94 Bulletin 94/33.

(56) List of documents cited in the search report:

Refer to the end of this publication

(60) References to other related national documents:

(71) Applicant(s): PASTEUR INSTITUTE private foundation recognized as public utility. - FR

(72) Inventor(s): ORTH GERALD - VOLPERS CHRISTOPH - STREECK ROLF

(73) Owner(s):

(74) Agent(s): GUTMANN ERNEST - PLASSERAUD YVES S.A.

US005981173

United States Patent [19]

Orth et al.

[11] Patent Number: 5,981,173

[45] Date of Patent: Nov. 9, 1999

[54] GENITAL HUMAN PAPILLOMAVIRUS TYPE 68A (HPV-68A), RELATED TO THE POTENTIALLY ONCOGENIC HPV-39

[75] Inventors: Gerard Orth, Sceaux, France; Sylvie Beaudenon, Highland Park, N.J.; Michele Longuet, Palaiseau, France

[73] Assignees: Institut Pasteur; Institut Nationale de la Sante Et de la Recherche Medicale, both of Paris, France

[21] Appl. No.: 08/815,667

[22] Filed: Feb. 11, 1997

Related U.S. Application Data

[60] Provisional application No. 60/011,650, Feb. 14, 1996, and provisional application No. 60/020,458, Feb. 15, 1996.

[51] Int. Cl.[6] C12Q 1/70; C12P 19/34; A61K 39/12; C12N 15/34

[52] U.S. Cl. 435/5; 435/6; 435/7.1; 435/320.1; 435/91.1; 536/23.72; 424/204.1; 424/229.1; 424/199.1

[58] Field of Search 424/199.1, 204.1, 424/229.1; 536/23.72; 435/5, 6, 7.1, 320.1, 91.1

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Longuet et al, 1996, Journal of Clinical Microbiology, 1996, vol. 34, No. 3, pp. 738–744.

Primary Examiner—Mary E. Mosher

Assistant Examiner—Ali R. Salimi

Attorney, Agent, or Firm—Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.

[57] ABSTRACT

The genomes of two novel human papillomavirus (HPV) types, HPV68 and HPV70, were cloned from a low grade cervical intraepithelial neoplasia and a vulvar papilloma, respectively, and sequenced. Both types are related to HPV39, a potentially oncogenic virus. HPV68 and HPV70 were also detected in genital intraepithelial neoplasia from three patients and one patient, respectively. Comparison with sequence data in the literature indicates that the subgenomic ME180-HPV DNA fragment, cloned from a carcinoma cell line, corresponds to an HPV68 subtype and that several HPV DNA fragments amplified by PCR from genital neoplasia represent worldwide distributed variants of HPV68 and HPV70.

13 Claims, 9 Drawing Sheets

* Confidential Treatment Requested

1-19

EXHIBIT B

PRODUCT SPECIFICATIONS, ANALYTICAL METHOD TRANSFER AND GMP MANUFACTURE OF HPV OLIGONUCLEOTIDES AND HPV TRANSCRIPTS

EXHIBIT B-1

Product Specification, Analytical Method Transfer and GMP Manufacture of HPV Reagent Products.

The product specifications detailed in this Exhibit (as of the Effective Date) are general in nature. During the period when ROCHE is supplying Notebook and Draft Production lots of HPV Reagent Products, specifications for the HPV Products will become more detailed. The Parties will from time to time amend this Exhibit to reflect the more detailed product specification.

1. Overview

This purchase and supply arrangement will consist of two phases:

(a) Technology Transfer
(b) Manufacture and Supply of HPV Reagent Products

Prior to initiation of manufacture of the first Notebook lot, GPRO and ROCHE will meet to review the manufacturing plan and the analytical methods to be employed. Thereafter and throughout the period when ROCHE is supplying and delivering the HPV Reagent Products for non-commercial use, GPRO and ROCHE will meet regularly as reasonably needed to review timelines, manufacturing processes, QC methods and product specifications.

2. GPRO's HPV Reagent Products Requirements

Total Number of Oligonucleotides per Individual HPV Test Quantity: Approx 30 different oligonucleotides:

Oligonucleotide Classification:

Group 1 – oligonucleotides containing up to 65 bases
Group 2 – oligonucleotides containing up to 30 bases
Group 3 – oligonucleotides containing up to 39 bases
Group 4 – oligonucleotides containing up to 65 bases

General Specifications: All phosphodiester, DNA, some oligos require 2' MeO

Amounts of Oligonucleotide

Group 1 – Approx 40mg per lot of 200,000 tests

Group 2 – Approx 20mg per lot of 200,000 tests

Group 3 – Approx 20mg for lots up to 1,000,000 tests

Group 4 – Approx 10mg per lot of 200,000 tests

Oligonucleotide Sequences: The specific sequences for each of the oligonucleotides for the HPV Reagent Products to be included in the HPV TMA Test Kits for use with TMA will be transferred to ROCHE during technology transfer.

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3. Technology Transfer

The Technology Transfer phase may require site visits by GPRO personnel to ROCHE. Topics to be covered could include but are not limited to raw material vendor specific requirements, synthesis method development, purity methods, and analytical methods. Completion of technology transfer is estimated at 6-8 weeks.

The following table lists the proposed analytical methods to be transferred to ROCHE for use in release testing of GMP material, as well as the approximate quantity of material required to perform these release tests. The analytical methods included in the following table have or will be validated by GPRO. For Notebook and Draft Production Lots, sequencing of the oligonucleotides for identification will be required.

Parameter	Analytical Method	Method Transfer Required	Sample Volume required for Analytical Test
Purity	HPLC	✔	TBD
Concentration	UV	✔	
Molecular Weight	MALDI-Tof	✔	

4. GMP Manufacture

ROCHE will provide GMP manufactured HPV Reagent Products (termed "Notebook ", "Draft Production" and "Production" lots) made to the agreed upon specifications and batch sizes, using the process description as provided by ROCHE and approved by GPRO. (Notebook lots may not include all required GMP documentation.) During Notebook Lot manufacturing, it is expected that ROCHE will concurrently develop GMP compliant systems and processes for the manufacturing of Production Lot oligonucleotides. GPRO may initiate ordering of Draft Production or Production Lot materials prior to the conclusion of Notebook Lot production. Subject to Section 4.2 of the Agreement, GPRO will allow a maximum of 120 calendar days from the time of order placement to receipt of Draft Production or Production Lot material.

If and to the extent that GPRO specifies or provides to ROCHE any method for oligonucleotide synthesis and/or oligonucleotide purification processes, GPRO shall provide to ROCHE any existing validation or verification of such methods. If and to the extent that ROCHE uses ROCHE's methods for oligonucleotide synthesis and/or oligonucleotide purification processes, ROCHE will provide a validation or verification plan for the oligonucleotide synthesis and oligonucleotide purification processes before initiating the manufacture of the first Notebook lot. These ROCHE validation and/or verification plans must be agreed upon by GPRO and ROCHE. HPV Reagent Products manufactured by ROCHE shall be delivered in accordance with the terms and conditions of the Agreement and, unless GPRO requests deferral of delivery pursuant to Section 4.4 of the Agreement, shall be delivered no more than four (4) months following the date of manufacture.

5. Packaging and Delivery

The packaging method will be by 35 ml aliquots in 50 ml Oakridge tubes (Fisher #05-529-1D). The HPV oligonucleotides will be diluted in PCR Grade water. The use of PCR grade water as diluent is

subject to GPRO review of ROCHE's water systems to be completed during the technology transfer process and prior to the initiation of the manufacture of the first Notebook Lot. Product must be labeled with applicable patent markings pursuant to Section 7.2 of the Agreement, oligonucleotide description, part number, batch number, manufacturing date, purity and concentration. Product must be stored at -15°C to -30°C prior to delivery. Product will be delivered over night on dry ice. Product must be delivered to GPRO in a frozen state.

6. Product Contact Surfaces:

GPRO requires all final oligonucleotide contact surfaces to be single-use to prevent any contamination. Examples of final oligonucleotide contact surfaces include but are not limited to laboratory glassware, purification columns, tubing, and diafiltration cassettes. GPRO reserves the right to designate such contact surfaces. GPRO will require a designated freezer for the storage of completed HPV Reagent Products.

7. Specifications

The following table outlines preliminary analytical tests and specifications that will be used for testing Notebook Lots of HPV Reagent Products. Specifications are set for each of the 4 different oligonucleotide groups. This testing will be conducted on Notebook lots for information purposes only. Also, a joint study will be conducted by ROCHE and GPRO on initial Notebook lots to determine the equivalency of the purity levels of the oligonucleotides as measured by ROCHE's QC methods compared with the purity levels as measured by GPRO's QC methods.

Final sequence and purity specifications will be set for each type of oligonucleotide manufactured in the Production lots. These final specifications will be based on information collected from Notebook and Draft Production manufacturing lots for each type of oligonucleotide.

Oligonucleotide Group	GPRO Target Purity*	Mass Specification**	Concentration Specification***
Group 1	≥ 80%	+/- 0.1% theoretical mass g/M	ROCHE QC value within 10% of ROCHE Mfg Value
Group 2	≥ 85%	+/- 0.1% theoretical mass g/M	ROCHE QC value within 10% of ROCHE Mfg Value
Group 3	≥ 80%	+/- 0.1% theoretical mass g/M	ROCHE QC value within 10% of ROCHE Mfg Value
Group 4	≥ 75%	+/- 0.1% theoretical mass g/M	ROCHE QC value within 10% of ROCHE Mfg Value

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***Purity as determined by GPRO using GPRO's standard QC testing methods for oligonucleotides including ion exchange and HPLC**

****Mass Specification determined by Maldi-Tof.**

***ROCHE's QC determined value for the concentration of each HPV oligonucleotide (as determined by UV measurement in OD units/mL) must be within 10% of ROCHE's manufacturing target value.

8. GMP Documentation

In order to ensure compliance with current GMP, and any other applicable regulatory requirements or guidelines, compliant documentation from batch records, analytical methods, final release testing, etc. will be generated specifically for HPV Reagent Products. GMP documentation, including batch records, will be available for GPRO review.

9. Quality Assurance

A Certificate of Analysis (C of A) and Material Safety Data Sheet (MSDS) will be provided for all HPV Reagent Products delivered. The Certificate of Analysis will contain applicable patent markings pursuant to Section 7.2 of the Agreement, the oligonucleotide description, including lot type, part number, batch number, manufacturing date, purity, concentration, manufacturing location and storage condition. Upon the request by ROCHE, GPRO will more specifically describe the content and form it requests for the C of A and MSDS.

EXHIBIT B-2

Product Specification, Analytical Method Transfer and GMP Manufacture of HPV RNA Transcript and HPV DNA Products

The product specifications detailed in this Exhibit (as of the Effective Date) are general in nature. The Parties will, from time to time, amend this Exhibit to reflect a more detailed product specification.

1. Overview

This purchase and supply arrangement will consist of 2 phases:

- Technology Transfer
- Manufacture and Supply of HPV Transcript Products

2. RNA Transcript AND HPV DNA Description

ROCHE will supply GPRO HPV Transcript Products for the following HPV types: 42, 35, 56, 43, 39, 33. In the event GPRO needs HPV Transcript Products for additional HPV types, ROCHE will reasonably consider making such HPV Transcript Products for GPRO.

The transcripts will include the E6 and E7 genes and a 100 base sequence of the L1 gene.
GPRO will supply ROCHE with the specific transcript sequences during the technology transfer phase.

In the event that Gen-Probe develops a HPV TMA Test kit directed at HPV viral DNA then ROCHE agrees to provide Gen-Probe with certain HPV DNA or fragments cloned into a suitable vector, in lieu of HPV RNA Transcripts. Such HPV DNA should be purified from the expression vector and be free of contaminating nucleases that could interfere with assay performance.

3. Technology Transfer

The following table lists the proposed analytical methods to be transferred to ROCHE for use in release testing of HPV RNA Transcript and HPV DNA Products, as well as the approximate quantity of material required to perform these release tests. The analytical methods included in the following table have or will be validated by GPRO. Completion of technology transfer is estimated at 6-8 weeks.

Parameter	Analytical Method	Method Transfer Required	Approx. Sample Quantity required for Analytical Test
HPV RNA Transcripts		☐	
Gel photo	Digital Image or Polaroid	✔	4 tubes @ 5 ug / tube
Molecular Weight	RNA Ladder Bands	✔	

Purity	PAGE (Polyacrylamide agarose Gel Electrophoresis)	✔	
Sequence	RNA Sequencing	✔	
HPV DNA		☐	
Gel Photo	Digital image or Polaroid	☐	
Purity	PAGE	☐	
Sequence	DNA Sequencing	☐	

Quantity required for analytical testing is subject to change

4. Manufacturing of HPV RNA Transcript and HPV DNA Products

The HPV RNA Transcript Products should be manufactured under GMP using the Ambion Megascript T7 kit for transcription and termination followed by the Qiagen Rnaeasy Mini Kit (or Ambion Megaclear kit) for purification. The yield from each lot of HPV Transcript Product must be greater than 100 micrograms of transcript.

HPV RNA Transcript and HPV DNA Products manufactured by ROCHE shall be delivered in accordance with the terms and conditions of the Agreement and, unless GPRO requests deferral of delivery pursuant to Section 4.4 of the Agreement, shall be delivered no more than four (4) months following the date of manufacture.

5. Packaging and Delivery

The packaging method will be in 0.5 ml aliquots in microcentrifuge tubes at a concentration of 5 ug/mL. Transcripts will be diluted in Rnase free water. Product must be labeled with applicable patent markings pursuant to Section 7.2 of the Agreement, transcript description, part number, batch number, manufacturing date, purity and concentration. Product must be stored at ≤ -65°C prior to delivery. Product will be delivered over night on dry ice. Product must be delivered to GPRO in a frozen state.

6. Specifications

Product specifications for transcripts and DNA will be 100% agreement with master sequence in areas specified by GPRO and fulfillment of order quantity.

QC analytical methods to be performed for product release will include the following methods:

- Photographic image of the PAGE gel for purposes including,
  - Molecular Weight by PAGE
  - Purity > 90% by PAGE

- Sequencing (100% agreement)

7. GMP Documentation

In order to ensure compliance with current GMP, and any other applicable regulatory requirements or guidelines, compliant documentation from batch records, analytical methods, final release testing, etc. will be generated specifically for the HPV RNA Transcript and HPV DNA Products. GMP documentation, including batch records, will be available for GPRO review.

8. Quality Assurance

A Certificate of Analysis (C of A) and Material Safety Data Sheet (MSDS) will be provided for all HPV RNA Transcript and HPV DNA Products delivered. The Certificate of Analysis will contain the applicable patent markings pursuant to Section 7.2 of the Agreement, ribonucleotide description, part number, batch number, manufacturing date, purity, concentration, manufacturing location and storage condition. Upon the request of ROCHE, GPRO will more specifically describe the contents and form it requests for the C of A and MSDS.

EXHIBIT C

TRANSFER FEES FOR HPV REAGENT PRODUCTS FOR NON-COMMERCIAL AND CLINICAL TRIAL USE

The Transfer Fee and order size for GPRO's purchase of HPV Reagent Products for Non-Commercial Use and Clinical Trial Use shall be as follows:

Manufacturing Process Designation	Overall Lot Size	Constituent Batch Sizes	Price Per Individual HPV Test Quantity
Notebook Lots	600,000	3 x 200,000	$2.00
Draft Production Lots and Production Lots	1,100,000	1 x 900,000 1 x 200,000	$2.50
" "	2,200,000	1 x 1,400,000 1 x 800,000	$1.60
" "	200,000	1 x 200,000	$ 8.40
" "	500,000	1 x 500,000	$ 4.80
" "	1,000,000	1 x 1,000,000	$1.80
" "	2,000,000	1 x 2,000,000	$ 1.30
" "	3,000,000	1 x 3,000,000	$ 1.00

"Notebook Lots" means HPV Reagent Product lots manufactured pursuant to and in accordance with ROCHE's Notebook Lot documentation practices for oligonucleotides intended for use solely in product development. The specifications for process and product, identity and purity tests for such HPV Reagent Product lots will be preliminary and subject to modification. Neither official Quality Control testing by ROCHE nor Quality Assurance release by ROCHE will be required for Notebook Lots. Certificate of Analysis indicating purity and identity is required.

"Draft Production Lots" means HPV Reagent Product lots manufactured pursuant to and in accordance with ROCHE's Draft Production Lot documentation practices. The specifications for process and product, identity and purity tests for such HPV Reagent Product lots will be preliminary and subject to modification. Manufacturing may be performed with generic batch record where redlining of manufacturing documents by the operator are acceptable. Neither official Quality Control testing by ROCHE nor Quality Assurance release by ROCHE will be required for Draft Production Lots. Certificate of Analysis indicating purity and identity is required.

"Production Lots" means HPV Reagent Product lots manufactured pursuant to and in accordance with ROCHE's GMP Production documentation practices, with full GMP manufacturing and testing with final process and product specifications. Official Quality Control testing and Quality Assurance release are required. All manufacturing processes and all test methods are validated and / or verified.