

DNA Synthesis for PCR

Quality Primer Synthesis In Your Own Lab: The First Step in Perfect PCR.

When your primer is right, PCR can deliver results in record time. When it's wrong, the time lost is gone forever. Flawless synthesis of well-designed primers is the first step toward perfect PCR. We guarantee primers produced on an Applied Biosystems 392 DNA/RNA Synthesizer to be $\geq 99.8\%$ chemically authentic, yet they are easy and affordable to make.



The 392 is fully automated, from initial phosphoramidite dilution through final cleavage from the synthesis support. It simultaneously synthesizes *both* PCR primers. Simply key in the sequences and

press "start synthesis." The 392 does the rest. And it can be upgraded easily from two to four columns as your needs grow.

Its 40-nmol synthesis scale on polystyrene supports reduces reagent use, increases the useful life of phosphoramidites by 50%, and yields a higher percentage of desired product than any alternative. Even desalting, the final preparation for PCR, is simple with our patented oligonucleotide purification cartridge (OPC™).

Says one user, "As long-time users of Applied Biosystems instruments and reagents, we have rated them 'excellent' for reliability and ease of use, as well as the high quality of synthesis."*

Wherever you are, our worldwide manufacturing and delivery network supplies fresh reagents and phosphoramidites without delay. As an Applied Biosystems customer, you also benefit from a broad

range of technical service and support.

Besides PCR primers, the 392 makes it easy to synthesize antisense oligonucleotides, ribozymes, and sequencing primers. Phone us to find out how the 392 can accelerate your research, and we'll send you a free copy of our new reference manual, *Evaluating and Isolating Synthetic Oligonucleotides*. Phone Applied Biosystems at: **Australia** (03) 808-7777, **Benelux** (0)3465-74868, **Canada** (800)668-6913, **France** (1) 49 90 18 00, **Germany** 0 61 51/87 94-0, **Italy** (02) 8912 6011, **Japan** (03) 3699-0700, **U.K.** (0925) 825650, **U.S.** (800) 345-5ABI.

 **Applied Biosystems**
A Division of Perkin-Elmer Corporation

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* Eva Kvist, Scandinavian Gene Synthesis AB, Køping, Sweden.

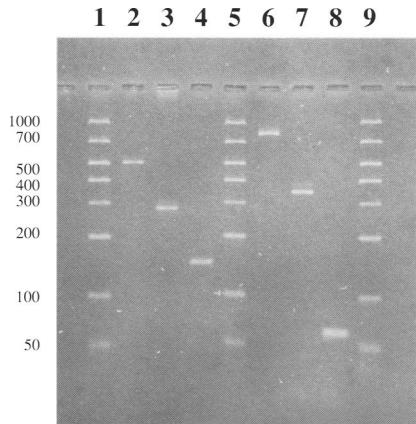
The GeneAmp® PCR process is covered by U.S. Patents owned by Hoffmann-LaRoche Inc.

and issued and pending patents owned by F. Hoffmann-LaRoche A.G.

GelMarker™

GelMarker™ is a molecular weight standard specifically designed to accurately quantitate yields and determine the size of PCR[†] products separated by gel electrophoresis.

- Ideal range of coverage for PCR products - 50 through 1000 bp
- Easy estimation of yield - each band contains 50 ng of DNA
- Ethidium bromide stains each band with equal intensity
- Ready to load - no preheating required
- Biotin and Digoxigenin labeled GelMarker™ also available
- Band sizes are exactly 50, 100, 200, 300, 400, 500, 700, and 1000 bp
- Seven bands spaced to easily plot in one log cycle from 100 to 1000 bp for more accurate size determination



Lane 1 5 μl of GelMarker™

Lane 2 500 bp

Lane 3 296 bp

Lane 4 138 bp

Lane 5 5 μl of GelMarker™

Lane 6 792 bp

Lane 7 365 bp

Lane 8 67 bp

Lane 9 5 μl of GelMarker™

4% agarose; NuSieveGTG™ : agarose 3:1

™GelMarker is a trademark of Research Genetics

™NuSieve is a trademark of FMC Corp.

†PCR is covered by U.S. patents issued to the Cetus Corp.

The use of digoxigenin in the labeling of oligonucleotides is licensed to Research Genetics from Boehringer Mannheim

GelMarker™ Ordering Information

50 assays (250 μl).....Catalog No. 701006.050.....\$77.00

100 assays (500 μl).....Catalog No. 701006.100.....\$137.00

Research Genetics

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Can Your PCR* Thermal Cycler Use Thin Wall Reaction Tubes?

Between the thermal cycler heat block and your polymerase chain reaction is a critical wall of polypropylene. With faster cycling times and more amplifications, a thin wall tube is an absolute requirement to see the reaction to completion.

Many thermal cyclers are designed for high efficiency reactions where heat transfer does not become the limiting factor in fast cycle times. Ask your thermal cycler manufacturer which tubes are recommended for their unit. Chances are, the recommendation will include Robbins Scientific.

*PCR patents are owned by Hoffmann-LaRoche Inc.

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Whether your cycler uses 0.2ml or 0.5ml thin wall tubes, Robbins Scientific can ship assorted colors in sterile or nonsterile packages.

For those laboratories engaged in large scale genomic studies, STRIP-EASE TUBES and disposable TRAYS, pre-loaded with 96 thin wall 0.2ml tubes, speed up loading and unloading thermal cycler wells.

Reader Service No. 304

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Editorial Office: Cold Spring Harbor Laboratory Press, 1 Bungtown Road, Cold Spring Harbor, New York 11724-2203. Phone: 516-367-8492; FAX 516-367-8532.

PCR Methods and Applications (ISSN 1054-9803) is published bimonthly for \$255 (U.S. institutional; \$270 R.O.W.), \$82.50 (individual making personal payment; \$97.50 R.O.W. surface, \$30 additional for airmail) by Cold Spring Harbor Laboratory Press, 1 Bungtown Road, Cold Spring Harbor, New York 11724. Second class postage pending is paid at Cold Spring Harbor and additional mailing offices. POSTMASTER: Send address changes to Cold Spring Harbor Laboratory, 10 Skyline Drive, Plainview, New York 11803-9729.

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STRATAGENE BRINGS BACK

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Stratagene Introduces the Opti-Prime™ PCR⁺ Optimization Kit

PCR primers and DNA templates vary in purity, GC content and amount of secondary structure. In addition, DNA may have chemical modifications, nucleic acid analogs or other characteristics that can inhibit amplification efficiency. To improve the yield and specificity of the desired PCR products, the buffer components of a specific amplification reaction can be modified. But the process is tedious and time-consuming.

Stratagene's Opti-Prime™ PCR optimization kit does it for you. This unique matrix of carefully designed buffers and PCR additives can greatly enhance the quality of PCR amplification reactions. Our Perfect Match® PCR Enhancer is included as one of the six PCR additives known to improve the specificity and overall vigor of PCR.

Order now and let Stratagene's Opti-Prime Kit add music to your amplifications.

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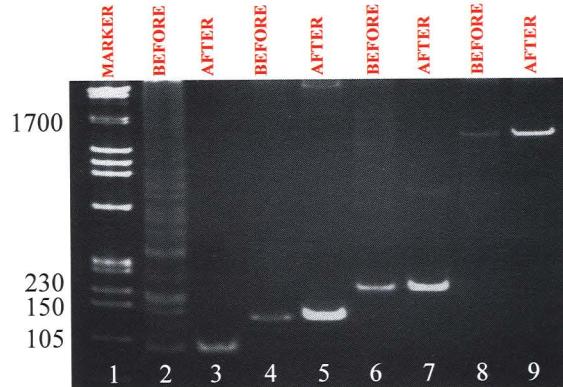
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Stratagene GmbH

Telephone: (01) 3641106

Telex: (01) 3657707

PCR OPTIMIZATION



Four primer/template sets were PCR-amplified using either standard *Taq* polymerase buffer (10mM Tris, 50mM KCl and 1.5mM MgCl₂) or individually optimized Opti-Prime™ buffer systems. Lane 1: 1 μ g of lambda Hind III/phi x 174 Hae III marker. Lanes 2&3: 105- bp PCR product of a human Gaucher's disease gene. Lanes 4&5: 150-bp PCR product of Bluescript® vector MCS. Lanes 6&7: 230-bp PCR product of an Epstein Barr viral nuclear antigen gene. Lanes 8&9: 1700-bp PCR product of a *lacZ* target gene from a transgenic mouse. Lanes 2,4,6 and 8 are of primer/template sets amplified using standard *Taq* polymerase buffer. Lanes 3,5,7 and 9 are of primer/template sets amplified using individually optimized Opti-Prime kit buffers.

*The PCR process is covered by patents owned by Hoffmann-La Roche Inc. Use of the PCR process requires a license.

3

THREE FOLD
REDUCTION IN
AMIDITE USAGE —
MORE ECONOMICAL
OLIGOS

BREAKTHROUGH IN PROCESS SCALE SYNTHESIS

OligoPilot™

OligoPilot™ Large Scale Oligo Synthesizer is designed for synthesis from 10 μmol to 400 μmol (up to 800 μmol capacity with high load support).

3

THREE FOLD
REDUCTION IN
SOLVENT USAGE —
REDUCED SOLVENT
DISPOSAL COST

5'-ATC GAA TGA GTT CCA GTT-3'

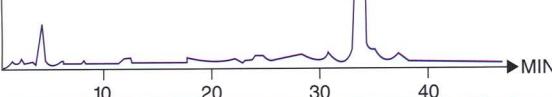
Column: Pep RPC HR5/5(C₁₈)

Buffers: A: 100mM TEAA,
5% Acetonitrile, pH 7.0

B: 100mM TEAA,
30% Acetonitrile, pH 7.0

Flow: 1.0 ml/min

Gradient: 0-100%



OligoPilot™ utilizes an innovative pump driven flow-through column design and a new polymer support matrix, Primer Support. The flow-through design gives you the following benefits:

- Significant reductions in amidite usage, 1.5 molar equivalents
- Fast detritylation, 2 min. at 200 μmol scale
- Short cycle times, 7 hours at 200 μmol for a 20-mer
- Reduced waste volume, 415 ml at 200 μmol scale
- Average yield per cycle of over 99%
- 12 amidite ports for DNA, RNA or modified amidites

The pump driven flow-through design ensures the active phosphoramidite concentrations remain high even at small molar excesses. This design also makes the most efficient use of other reagents and allows for rapid reagent change at up to 75 ml per minute.

Primer Support contributes to the overall performance due to its hydrophobic nature. Its hydrophobicity ensures that any water introduced with the oxidation step does not remain in the system, reducing coupling efficiency in later steps. The lack of labile sites also minimizes spontaneous chain elongation off the support which is sited for silica based supports.

OligoPilot is fully programmable via an external computer. In addition, the computer tracks reagent usage and identifies the batch numbers for each reagent used for each oligo synthesis.

The on-line trityl monitor provides continuous display of coupling efficiency of each step. In the event of a poor coupling, the monitor can stop the synthesis before additional reagents are wasted.

Lab scale synthesis users can enjoy similar benefits of Primer Support and the pump driven flow-through design with the Gene Assembler® DNA/RNA Synthesizer.

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Dual Experiment Flexibility: Two Thermal Blocks in a Smaller Unit

Economy of scale is something you'll appreciate as soon as PowerBlock is in your lab. Small footprint and light weight make it a compact and transportable "workhorse". You'll be able to incubate up to 30 samples at once, or perform two totally independent experiments simultaneously using up to 15 samples in each experiment.

The Accuracy of Actual Sample Temperature Monitoring

The PowerBlock employs a fast-response, thin-wire thermocouple for pin-point uniform temperature control. This monitor is placed in an actual microfuge tube and therefore measures actual internal sample temperatures, ensuring optimum reproducibility.

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per block***



POWERBLOCK: THE NEW ECONOMY OF SCALE

Faster-Cycling Peltier Heat Pump Operation

Ericomp's state-of-the-art Peltier-effect heat pump design delivers rapid heating and cooling in a temperature range of 4 to 100 degrees C. Ramp speeds average 1.5 degrees/sec. All this is accomplished without moving parts, expensive heavy compressors or robotic mechanisms.

Eliminating the Need for Oil

Ericomp's powerful feature, the optional Evaporation Control



Device (ECD), makes the **EasyCycler™ Series** even easier to use. The ECD will eliminate placing and extracting mineral oil overlays used during DNA amplification. Each sample can be extracted with minimal sample loss, and you have the option of using less reagent by running smaller samples.

Highly Reliable

Thousands of scientists use Ericomp's rugged "workhorse" temperature cyclers because of their proven reliability and durability. Ericomp's exclusive 3-year warranty is standard, and our customer service is unmatched in the industry.

.2ml Microcentrifuge Tube or .5ml Microcentrifuge Tube Configuration

The PowerBlock System can be configured with either a .2ml block or a .5ml block, or one block of each in the same unit! No other cycling system can match this kind of sample format diversity.

Attractive Price

Economy of scale means your budget can handle it. So, if your lab needs an economical, yet accurate and reliable answer to temperature cycling, the new, compact, cost-effective PowerBlock System is the ideal solution. Feature for feature, and dollar for dollar, we invite your comparison.

*Total unit cost: \$3295.00,
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The sharply curved bill of the white-tipped sickle-billed hummingbird is specifically adapted to probe the delicate tubular flowers of heliconia plants for the nectar on which the creature survives.

High-performance Boehringer Mannheim *Taq* DNA polymerase is designed and tested with an equally specific goal in mind: to produce absolutely specific amplification products in your polymerase chain reactions.

Each lot of *Taq* polymerase undergoes a unique self-priming assay to assure that the enzyme is essentially free of endogenous DNA fragments. Additional testing makes sure that contaminating exonucleases and endonucleases are also not present.



Specific amplification of a single-copy β -globin gene (1.5 kb) from 100 ng of human genomic DNA using various unit (U) quantities of Boehringer Mannheim *Taq* polymerase.

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Digene SHARP Signal System Probe/Primer Sets are available to detect HIV, HBV, HCV, CMV, Mtb, and other infectious disease targets.

For research use only. The Polymerase Chain Reaction (PCR) process is covered by U.S. patents owned by Hoffman-LaRoche.

Product news . . .

Stratagene's DNA MicroExtraction Kit

The new DNA MicroExtraction Kit from Stratagene allows isolation of DNA in just 1 hr from as little as 1 μ l of whole blood. The kit consistently extracts DNA from a host of different blood samples. PCR fragments of diverse sizes can be generated from the isolated DNA by use of various amplification primers. Researchers using the kit follow a simple protocol that eliminates the time-consuming mixing steps of conventional extraction methods and avoids the dangers and toxic-waste disposal problems of phenol/chloroform. The kit contains all the reagents needed to lyse blood cells and isolate purified DNA (enough for 100 reactions).

Contact: Stratagene, 11011 North Torrey Pines Road, La Jolla, California 92037; 1-(800)424-5444; (619)535-5400. Reader Service No. 312.

LabIntelligence's high performance gel electrophoresis (HPGE) system

LabIntelligence introduces the first fully integrated, computer-controlled electrophoretic system for rapid separation, identification, and retrieval of a wide range of biomaterials. The 1000-volt model HPGE 1000 automatically delivers nucleic acid, protein, viral, and other samples onto an agarose or polyacrylamide gel and then maintains a precise, computer-regulated separation environment with respect to voltage, current, buffer conditions, and temperature. Dur-

ing the run, it periodically scans the gel and displays fluorescently labeled zones, estimating molecular sizes and printing results. The HPGE 1000 also has preparative capabilities. It can automatically retrieve gel zones in seconds for use in subsequent experiments. In addition, it can electrophoretically concentrate dilute sample components in large volumes prior to separation. The complete system includes novel gels and optimized protocols for applications in life science research, genome mapping, biotechnology process and quality control, clinical diagnostics, and forensic analysis.

Contact: LabIntelligence, 191 Jefferson Drive, Menlo Park, California 94025-1114; (415)324-9005; FAX(415)324-9008. Reader Service No. 313.

DNA quantitative standards kit for ethidium bromide-stained gels

GenSura Laboratories, Inc., now offers its new Quantitation Standards kit, which provides separate tubes (sufficient for >200 loadings) containing 10 μ g each of purified and accurately quantified DNA fragments of 200, 500, and 1000 bp. This kit is ideal for quantifying PCR fragments in all common size ranges. The user can prepare custom standards by combining equal or different quantities of each fragment in the same sample well. Alternatively, the user can run the standards separately as desired for maximum utility. The range of fragment sizes provides optimal conditions for the problematic visual estima-



Product news features newly available equipment, laboratory equipment, and software that may be of interest to the readers of this journal. Endorsement by *PCR Methods and Applications* or Cold Spring Harbor Laboratory is not implied. Readers may obtain further information regarding these products by entering the appropriate numbers on the postage-free Reader Service Card included in this issue.

tion of both sharp and diffuse DNA bands. **Contact:** GenSura Laboratories, Inc., 2640 Del Mar Heights Road, Suite 219, Del Mar, California 92014; 1-(800)-GENSURA; (619)535-0044; FAX(619)535-0899. Reader Service No. 314.

New GeneAmplimer HLA DRB Probe Set I for sensitive, reproducible PCR-based tissue typing

Perkin-Elmer's new GeneAmplimer HLA DRB Biotinylated Probe Set I and Probe Set II provide sensitive, reproducible PCR-based analysis of human leukocyte antigen (HLA) class II loci used in tissue typing research, as well as in parentage testing, forensic analysis, and human cell-line tracking. Superior to traditional tissue typing by serology, these probes enable users to distinguish 60 DRB1 alleles in every possible heterozygous combination. With the GeneAmplimer HLA DRB Probe Set I, samples need only DNA, not class II positive cells. The typing is reproducible and shows differences in alleles and hybridization patterns for every type. Complete protocols are included in the set for conducting PCR-based HLA typing. In addition, the reagents are synthetic, thus eliminating the inconsistency associated with the use of antisera. Perkin-Elmer's corresponding GeneAmplimer HLA DRB Allele-specific Primer Set makes detection of HLA class II loci easy, reliable, and sensitive when used with the probe sets. They can also be used for the analysis of HLA polymorphisms or to study the relationship between HLA variants and disease susceptibility.

Contact: The Perkin-Elmer Corporation, 761 Main Avenue, Norwalk Connecticut 06859-0310; (203)761-2574. Reader Service No. 315.

Automated DNA purification of CVS and amniotic fluid

Purification of DNA from chorionic villi samples (CVS) and direct amniotic fluid, usually a tedious manual procedure, is now a fully automated process on the Applied Biosystems GENEPURE 341 Nucleic Acid Purification System. The GENEPURE also provides improved reliability and consistency for small-sample extraction, while reducing the risk of sample mix-up and exposure to toxic substances. Isolating human DNA from chorionic villi and amniotic samples has

usually been difficult because the available sample is often limited. The process can also be time consuming: The amniocytes in amniotic fluid, for example, must be cultured for several weeks prior to purification to obtain sufficient DNA. PCR-based testing has enabled researchers to obtain data from smaller starting samples than was previously possible. These samples require a highly efficient method purification; ideally one that also permits purified DNA to be resuspended in a very small volume. The GENEPURE offers two automated chemistry options, standard and Fast Cycle, for purifying small quantities of DNA that is suitable for both PCR and Southern blot analysis. The stringency of the standard phenol/chloroform method is recommended for all samples and sizes. It yields highly purified DNA that is suitable for any type of analysis. Because of their small size and relatively low protein content, CVS and amniotic fluid are also good candidates for the Fast Cycle chemistry, a rapid, nonorganic alternative.

Contact: Applied Biosystems, 850 Lincoln Centre Drive, Foster City, California 94404; (415)570-6667; FAX (415)572-2743. Reader Service No. 316.

New 5'-AmpliFINDER RACE kit from CLONTECH

CLONTECH introduces its new 5'-AmpliFINDER RACE kit, designed to allow efficient PCR amplification of the 5' ends of cDNAs. Obtaining the 5' end coding region of a gene is critical for gene expression and structural studies. The 5' sequences, however, are often difficult to obtain, even after weeks or months of screening cDNA libraries. The 5'-AmpliFINDER RACE kit simplifies this process. In the 5'-AmpliFINDER method, cDNA is first synthesized from poly(A)⁺ RNA by use of a gene-specific primer. An AmpliFINDER anchor oligonucleotide is then ligated to the cDNA—the AmpliFINDER anchor is modified with an amino group to prevent self-ligation and contains an EcoRI for use in cloning to amplified fragments. The anchor-ligated cDNA is then amplified by PCR, with the AmpliFINDER anchor primer and a nested gene-specific primer. PCR products can be easily cloned for obtaining the sequence of the 5' end of the cDNA. The 5'-AmpliFINDER RACE kit provides an advantage over the original 5'-RACE

method, which requires homopolymeric tailing, an often inefficient and problematic step. Each 5'-AmpliFINDER RACE kit contains reagents for 10 cDNA syntheses, 20 anchor ligations, and several control reactions. A complete protocol includes a troubleshooting guide, discussions on primer design, control reactions, and expected results.

Contact: CLONTECH Laboratories, INC., 4030 Fabian Way, Palo Alto, California 94303; (800)662-CLON; (415)424-8222. Reader Service No. 317.

TAQuence cycle sequencing kit

USB offers the TAQuence cycle sequencing kit, which allows the determination of DNA sequence with limiting amounts of template DNA. The kit allows sequencing of as little as 10-100 ng of template DNA, including M13, plasmid, phagemid, PCR products, etc. With this method alkaline denaturation of plasmid DNA is unnecessary. DNA synthesis is carried out in successive cycles of denaturation, annealing, and synthesis by use of a 5'-end-labeled primer in a thermal cycler. DNA synthesis catalyzed by *Taq* DNA polymerase initiates at the 3' terminus of annealed primers and continues until chain growth is terminated by a dideoxynucleotide. The synthesis/denaturation cycle is repeated in the thermal cycler until product sufficient to detect on a sequencing gel has accumulated. The TAQuence cycle sequencing kit contains enzymes and reagents sufficient for end-labeling 100 sequencing primers and for 100 sequences (400 reactions).

Contact: United States Biochemical, P.O. Box 22400, Cleveland, Ohio 44122; (800)321-9322; FAX (800)535-0898. Reader Service No. 318.

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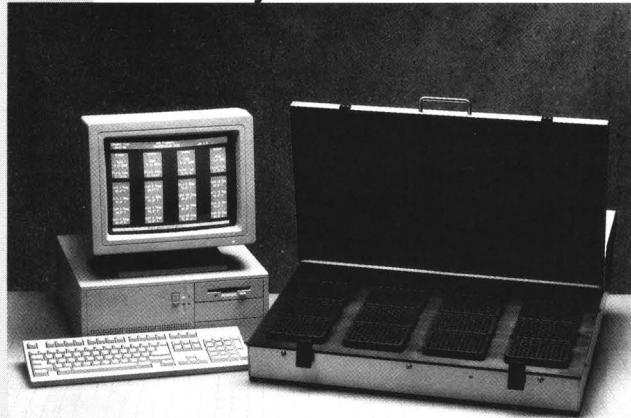
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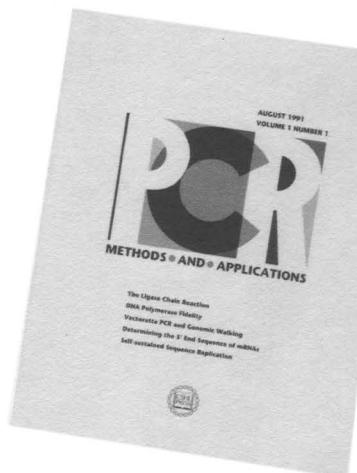
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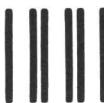
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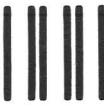
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