Appendix F
Acronyms and Glossary

Acronyms

-/-	-negative CF carrier/negative CF carrier (couple)
+/-	—positive CF carrier/negative CF carrier (couple)
+/+	—positive CF carrier/positive CF carrier (couple)
621 +1 G---›T	—a CF mutation
A	—adenine
AAP	—American Academy of Pediatrics
ABMG	—American Board of Medical Genetics
ACOG	—American College of Obstetricians and Gynecologists
ADA	—Americans With Disabilities Act of 1990
AFP	—alpha-fetoprotein
AHCPR	—Agency for Health Care Policy and Research
AIDs	—acquired immunodeficiency syndrome
AMA	—American Medical Association
AMP	—adenosine rnonophosphate
APKD	—adult polycystic kidney disease
ARMs	—arnpliflcation refractory mutation system
ASHG	—American Society of Human Genetics
ASO	—allele-specific oligonucleotide
ATP	—adenosine triphosphate
BABI	-blastomere analysis before implantation
Bart's	-St. Bartholomew's Hospital (London)
BC/BS	—Blue Cross and Blue Shield
C	-cytosine
Ca^{2+}	-calcium ion
CAMP	-cyclic adenosine monophosphate
CAP	--College of American Pathologists
CDHS	-California Department of Health Services
CF	-cystic fibrosis
CF Trust	-Cystic Fibrosis Research Trust (United Kingdom)
CFF	---Cystic Fibrosis Foundation
CFR	-Code of Federal Regulations
CFTRr	-cystic fibrosis transmembrane conductance regulator
CHAMPUS	-Civilian Health and Medical Program of the Uniformed Services
Cl-	-chloride ion
CLIA	-Clinical Laboratory Improvement Amendments of 1988
CORN	-Council of Regional Networks for Genetic Services
CVS	--chononic villus sampling
DF508	-delta F508 (most prevalent CF mutation)
DF508+6-12	-delta F508 plus six to 12 additional CF mutations
D1507	—a CF mutation
DHHS	—U.S. Department of Health and Human Services
DNA	-deoxyribonucleic acid
DNase	-deoxyribonuclease
DOD	—US. Department of Defense
DOE	—U.S. Department of Energy
EEOC	—U.S. Equal Employment Opportunity Commission
ELSI	—Ethical, Legal, and Social Issues Programs (NIH or DOE)
ERXSA	—Employee Retirement income Security Act of 1974
FCC	—Federal Communications Commission
FDA	—U.S. Food and Drug Administration
FFDCA	—Federal Food, Drug, and Cosmetic Act of 1938
FR	—Federal Register
G	—guanine
G542X	—a CF mutation
G551D	—a CF mutation
GAO	--General Accounting Office
GI	—gastrointestinal
GP	—general practitioner (United Kingdom)
Hb	-hemoglobin
HCFA	—Health Care Financing Administration
HexA	-hexosaminadase A
HHMI	—Howard Hughes Medical Institute
HIAA	—Health Insurance Association of America
HMO	—health maintenance organization
HSRC	—Health Services Research Committee (MRC; United Kingdom)
HSRP	—Health Services Research Panel (MRC; United Kingdom)
HUGA-1	—Human Genome Analysis System (Japan)
IDE	—Investigational Device Exemption
IRT	—immunoreactive trypsin
I v	—intravenous
kb	—kilobase(s); 1,000 base pairs
L	—liter
LCR	—ligase chain reaction
MCH	—Maternal and Child Health (Federal block grant)
MCV	—mean corpuscular volume
MDA	—Medical Device Amendments of 1976
MDR	—medical devices reporting (1984 regulation)

mg	—milligram
MHSS	—Military Health Services System
MIB	—Medical Information Bureau, Inc.
mmol	—millimnole
MRC	—Medical Research Council (United Kingdom)
mRNA	—messenger ribonucleic acid
MSAFP	—maternal serum alpha-fetoprotein
N1303K	—a CF mutation
Na^+	—sodium ion
NCHGR	—National Center for Human Genome Research (NIH)
NHLBI	—National Heart, Lung, and Blood Institute (NIH)
NHS	—National Health Service (United Kingdom)
NICHD	—National Institute of Child Health and Human Development (NIH)
NIDDK	—National Institute of Diabetes and Digestive and Kidney Diseases (NIH)
NIH	—National Institutes of Health
NRC	—National Research Council
NSF	—National Science Foundation
NSGC	—National Society of Genetic Counselors
NTD	-neural tube defect
NTSAD	—National Tay-Sachs and Allied Diseases Association
OTA	-Office of Technology Assessment
PCR	—polymerase chain reaction
PMA	—premarketing approval application
PPO	—preferred provider organization
PT	—physical therapy
R553X	—a CF mutation
RAC	—Recombinant DNA Advisory Committee (NIH)
RFA	—request for applications
RFLP	—restriction fragment length polymorphism
RNA	—ribonucleic acid
SMDA	-Safe Medical Devices Act of 1990
SPRANS	-Special Projects of Regional and National Significance
T	-thymine
UCLA	—University of California, Los Angeles
W1282X	—a CF mutation

Glossary of Terms

Adverse selection: The tendency of persons with poorer than average health expectations to apply for or continue insurance to a greater extent than persons with average or better health expectations. Also known as "antiselection."

Amino acid: Any of a group of 20 molecules that combine to form proteins in living things. The sequence of amino acids in a protein is determined by the genetic code.

Amniocentesis: The most widely used technique of prenatal diagnosis. Cells shed by the developing fetus are extracted from a sample of amniotic fluid withdrawn from the expectant mother's uterus at about 16 weeks of gestation by means of a hypodermic needle. The cells are cultured and then tested for chromosomal defects. In addition, scientists can now analyze the DNA of these cells directly, identifying specific genetic errors.

Allele: Alternative form of a genetic locus (e.g., at a locus for eye color there might be alleles resulting in blue or brown eyes); alleles are inherited separately from each parent.

Allele-specific **oligonucleotide** (ASO) **probe: Probes that are** able to exactly match the nucleotide sequence of a portion of a gene, detecting even single-base differences.

Automation: Technology, such as robotics, developed to increase the speed, volume, and accuracy of routine DNA diagnostic procedures.

AutoradiogPam: An x-ray film image showing the position of radioactive substances. Sometimes called "autorad."

Autoradiograph: See *autoradiogram.*

Autoradiography: A process for identifying radioactively labeled molecules or fragments of molecules.

Autosome: Chromosome not involved in sex determination. In a complete set of human chromosomes, there are 44 autosomes (22 pairs).

Base pair: Two complementary nucleotides held together by weak bonds. Two strands of DNA are held together in the shape of a double helix by the bonds between base pairs. The base adenine pairs with thyrnine, and guanine pairs with cytosine.

ß-thalassemia: An autosomal recessive disorder affecting the red blood cells, resulting in anemia, infections, growth retardation, andothercomplications. ß-thalassemia predominantly occurs among individuals of Mediterranean, Middle Eastern, Asian Indian, Chinese, Southeast Asian, and African descent.

Blot: See *Southern blot.*

Buccal: Relating to the inside of the cheek. A buccal swab collects cells from the inside of the cheek for CF mutation analysis.

Carrier: An individual apparently normal, but possessing a single copy of a recessive gene obscured by a dominant allele; a heterozygote.

Cell: The smallest component of life capable of independent reproduction and from which DNA can be isolated.

Chest physical therapy (chest PT): A cornerstone of CF therapy that moves the mucus blocking major air passages out of the lungs. One form of chest PT is bronchial drainage, during which an individual claps on the chest or back of the patient who is usually lying on a table or over a couch, to loosen mucus that the patient coughs up.

Chorionic **villus sampling** (CVS): A method of prenatal diagnosis undertaken as early as the 9th week of pregnancy. Fetal cells from chorionic villi (protrusions of a membrane, called the chorion, that surround a fetus during early development) are suctioned out through the uterus and their DNA is analyzed.

Chromosomal aberration: An abnormal chromosomal complement resulting from the loss, duplication, or rearrangement of genetic material.

Chromosome: A threadlike structure that carries genetic information arranged in a linear sequence. In humans, it consists of a complex of nucleic acids and proteins.

Cloning: The process of asexually producing a group of cells (clones), all genetically identical to the original ancestor. In recombinant DNA technology, the process of using a variety of DNA techniques to produce multiple copies of a single gene or segment of DNA.

Community rating: A method of determining premium rates based on the allocation of total costs without regard to past group experience, Community rating is required of federally qualified health maintenance organizations.

Complementary DNA (cDNA): DNA synthesized from a messenger RNA template; the single-strand form is often used as a probe in physical mapping.

Confidentiality: A fundamental component of the health care provider-patient relationship in which the professional has the duty to keep private all that is disclosed by the patient.

Consanguineous: Related by blood or origin, rather than by marriage.

Cystic fibrosis (CF): A life-shortening, autosomal recessive disorder affecting the respiratory, gastrointestinal, reproductive, and skeletal systems, as well as the sweat glands. CF is caused by mutations in the CF gene that affect the gene product, cystic fibrosis transmembrane conductance regulator. Individuals with CF possess two mutant CF genes.

Cystic fibrosis carrier: An individual who possesses one CF mutation and one normal CF gene. CF carriers manifest no symptoms of the disorder. See *carrier.*

Cystic fibrosis carrier screening: The performance of tests on persons for whom no family history of CF exists to determine whether they have one aberrant CF gene and one normal CF gene. Compare cystic *fibrosis screening.*

Cystic fibrosis screening: The performance of tests to diagnose the presence or absence of the actual disorder, in the absence of medical indications of the disease or a family history of CF. This type of diagnostic screening usually involves newborns, but is rare except in Colorado and Wisconsin. Compare *cysticfibrosis carrier screening.*

Cystic fibrosis transmembrane conductance regulator (CFTR): The CF gene product, which regulates chloride (Cl-) conductance and might be a Cl^- ion channel, the structure that governs Cl^- entry and exit in the cell. CFTR produced by a mutant CF gene is frequently impaired, resulting in the medical manifestations of CF in affected individuals.

DF508: A three base pair deletion in the CF gene that results in a faulty CF gene product (i.e., a flawed CFTR). This mutation results in the deletion of one amino acid, phenylalanine, at position number 508 in CFTR. DF508 is the most common mutant allele among the more than 170 mutations identified in the CF gene.

Deoxyribonucleic acid (DNA): The molecule that encodes genetic information. DNA is a double-stranded helix held together by weak bonds between base pairs of nucleotides.

Discrimination: Differential treatment or favor with a prejudiced outlook or action.

Dominant: An allele that exerts its phenotypic effect when present either in homozygous or heterozygous form.

Dot blot: A variation of Southern blotting that involves placing DNA into discrete spots on a nylon membrane. A probe or probes can be hybridized to the membrane and diagnosis made rapidly.

DNA: See *deoxyribonucleic acid.*

DNA **analysis:** A direct examination of the genetic material, DNA, to reveal whether a individual has a CF mutation. Also known as *DNA test* and *DNA assay.*

DNA **band: The** visual image, e.g., on a autoradiogram or an ethidium bromide stained gel, that represents a particular DNA fragment.

DNA **probe:** Short segment of DNA labeled with a radioactive or other chemical tag and then used to detect the presence of a particular DNA sequence

through hybridization to its complementary sequence.

DNA sequence: Order of nucleotide bases in DNA.

Double helix: The ladder-like shape formed by two linear strands of DNA bonded together.

Electrophoresis: Technique used to separate molecules such as DNA fragments or proteins. Electric current is passed through a gel and the fragments of DNA are separated by size. Smaller fragments migrate farther than larger pieces.

Enzyme: A protein that acts as a catalyst, speeding the rate at which a biochemical reaction proceeds, without being permanently altered or consumed by the reaction so that it can act repeatedly.

Epidemiology: The scientific study of the distribution and occurrence of human diseases, health conditions, and their determinants.

Eugenics: Attempts to improve hereditary qualities through selective breeding.

Exocrine **glands:** Glands that secrete into ducts or onto specific organ surfaces. Exoerine glands are classified as serous (producing a watery substance) or mucous (producing a viscous substance). CF affects both types, increasing the salt content of serous secretions and diminishing the salt content of mucus secretions. Mucous exoerine glands from individuals with CF then produce thicker than normal secretions leading to obstruction of the glands' ducts. Examples of exocrine glands include lacrimal (tear) glands, sweat glands, and part of the pancreas.

Exons: The protein-coding DNA sequences of a gene. Compare *introns.*

Frequency: The number of occurrences of a given allele within a given population.

Gel: The semi-solid matrix (e.g., agarosegeloracrylamide) used in electrophoresis to separate molecules.

Gene: The fundamental physical and functional unit of heredity. A gene is an ordered sequence of nucleotide base pairs to which a specific product or function can be assigned.

Gene mapping: Determining the relative locations of different genes on chromosomes.

Gene therapy: The deliberate administration of genetic material into the cells of a patient with the intent of correcting a specific genetic defect.

Genetic code: The sequence of nucleotides, coded in triplets along the mRNA, that determines the sequence of amino acids in protein synthesis. The DNA sequence of a gene can be used to predict the mRNA sequence, and this genetic code can in turn be used to predict the amino acid sequence.

Genetic counseling: A clinical service involving educational, informational, and psychosocial elements to provide an individual (and sometimes his or her family) with information about heritable conditions. Genetic counseling is performed by genetics specialists, including physicians, Ph.D. clinical geneticists, genetic counselors, nurses, and social workers.

Genetic screening: The analysis of samples from asymptomatic individuals with no family history of a disorder, groups of such individuals, or populations.

Genetic testing: The use of specific assays to determine the genetic status of individuals already suspected to be at high risk (e.g., family history or symptoms) for a particular inherited condition.

Genetics: The study of the patterns of inheritance of specific traits.

Genome: All the genetic **material in the** chromosomes of a particular organism; its size is generally given as its total number of base pairs. The human genome is **3.3** billion base pairs.

Genotype: The genetic constitution of an organism, as distinguished from its physical appearance, or phenotype.

Health maintenance organization (HMO): A health care organization that serves as both payer and provider of comprehensive medical services, provided by a defined group of physicians to an enrolled, fee-paying population.

Hemoglobin **(Hb):** A protein that carries oxygen in red blood cells. Sickle cell and thalassemia mutations affect hemoglobin.

Heterozygote: A heterozygous individual, such as a CF carrier.

Heterozygous: Having two different alleles at a particular locus.

Homozygote: A homozygous individual.

Homozygous: Having the same alleles at a particular locus.

Hybridization: The process of joining two complementary strands of DNA, or of DNA and RNA, together to form a double-stranded molecule.

Immunoreactive trypsin (IRT) test: An assay that measures levels of pancreatic trypsin, a digestive enzyme. As a protocol for newborn CF screening, a drop of blood is isolated on a card, dried, and chemically analyzed to detect elevated levels of the enzyme. It is not intended to be a diagnostic test.

In **vitro:** Literally, ''in glass,' pertaining to a biological process or reaction taking place in an artificial environment, usually a laboratory.

In vivo: Literally, "in the living," pertaining to a biological process or reaction taking place in a living cell or organism.

Introns: DNA sequences interrupting the protein-coding DNA sequences of a gene that are transcribed into mRNA, but are spliced out of the rnRNA before the rnRNA is translated into protein. Compare *exons.*

Karyotype: A photomicrograph of an individual's chromosomes arranged in a standard format showing the number, size, and shape of each chromosome.

Ligase chain reaction (LCR): An in vitro process that amplifies only the region of DNA directly underneath the known sequence to make millions of copies of this sequence. Mutations differing by a single base can be easily detected with this technique.

Linkage: The proximity of two or more markers (e.g., genes, RFLP markers) on a chromosome. The closer together the markers are the lower the probability that they will be separated during meiosis, and hence the greater the probability that they will be inherited together.

Linkage analysis: The process of studying DNA markers **to** trace the transmission of a particular gene and a specific mutation in **a** particular family. This can be performed only in families with a living CF affected member or from DNA samples stored from a deceased affected family member.

Locus: A specific, physical position on a chromosome.

Marker: A stretch of DNA with a known location on a chromosome that is used as a point of reference when mapping another locus. Markers can be important to linkage analysis and diagnosing genetic disease,

Meiosis: The process of reduction of genetic material and cell division in the diploid progenitors of sex cells. Meiosis results in four, rather than two, daughter cells, each with a single set of chromosomes.

Messenger RNA (mRNA): A class of RNA produced by transcribing the DNA sequence of a gene. An mRNA molecule is involved in translating instructions from the DNA sequence into proteins.

Mutation: Changes in the composition of DNA.

Nucleotide: The unit of DNA consisting of one of four bases—adenine, guanine, cytosine, or thymine-attached to a phosphate-sugar group. The sugar group is deoxyribose in DNA. In RNA, the sugar group is ribose and the base uracil substitutes for thymine.

Open enrollment: A health insurance enrollment period during which coverage is offered regardless of health status and without medical screening. Open enrollment periods are characteristic of some BC/BS **plans** and HMOs.

Phenotype: The appearance of an individual or the observable properties of an organism that result from the interaction of genes and the environment. Compare *genotype.*

Polymerase chain reaction (PCR): An in vitro process through which repeated cycling of the reaction reproduces a specific region of DNA between two sites, yielding millions of copies from the original.

Polymorphism: The existence of more than one form of a genetic trait.

Preexisting condition: A condition existing before an insurance policy goes into effect and commonly defined as one which would cause an ordinarily prudent person to seek diagnosis, care, or treatment.

Proband: The individual in a family first identified as manifesting a given heritable trait.

Probe: A short segment of DNA tagged with a reporter molecule, such as radioactive phosphorus (32P), used to detect the presence of that particular complementary DNA sequence.

Protein: A biological molecule whose structure is determined by the sequence of nucleotides in DNA. Proteins are required for the structure, function, and regulation of cells, tissues, and organs in the body.

Rated premium: A premium with an added surcharge that is required by insurers to cover the additional risk associated with certain medical conditions. Rated premiums usually range from 25 to 100 percent more than the standard premium.

Recombinant DNA technology: Processes used to form a DNA molecule through the union of different DNA molecules, but often commonly used to refer to any techniques that directly examine DNA.

Recessive: An allele that exerts its phenotypic effect only when present in homozygous form, otherwise being masked by the dominant allele,

Reliability: The ability of a test to accurately detect that which it was designed to detect and to do so in a consistent fashion.

Replication: The synthesis of new DNA from existing DNA. PCR is an in vitro technology based on principles of replication.

Restriction endonuclease: An enzyme that has the ability to recognize a specific DNA sequence and cut it at that sequence.

Restriction **enzyme: See** *restriction endonuclease.*

Restriction fragment length polymorphism (RFLP): Variations in the size of DNA fragments produced by a restriction endonuclease at a polymorphic locus.

Restriction fragment length polymorphism (RFLP) analysis: DNA technique using single-locus or multilocus probes to detect variation in the DNA sequence by revealing size differences in DNA fragments produced by the action of a restriction enzyme. See *restriction fragment length polymorphism.*

Reverse dot blot: Blotting in which allele-specific oligonucleotides (ASOs) are immobilized on the membrane. Key segments of the individual's unknown DNA are then amplified, labeled, and hybridized to the probes on the membrane.

Ribonucleic acid (RNA): A chemical found in the nucleus and cytoplasm of cells that plays an important role in protein synthesis and other chemical activities of the cell. The structure of RNA is similar to that of DNA. There are several classes of RNA molecules, including messenger RNA, transfer RNA, ribosomal RNA, and other small RNAs, each serving a different purpose.

RNA: See *ribonucleic acid.*

Sensitivity y: The ability of a test to identify correctly those who have a disease.

Sex chromosomes: The X and Y chromosomes in human beings that determine the sex of an individual. Females have two X chromosomes in somatic cells; males have an X and a Y chromosome.

Sickle cell anemia: An autosomal recessive disorder affecting red blood cell flow through the circulatory system, causing complications in numerous other organ systems. Sickle cell anemia predominantly occurs in individuals of African descent.

Sickle cell trait: The heterozygous state of sickle cell anemia; sickle cell carrier status.

Single-gene disorder: Hereditary disorder caused by a single gene (e.g., cystic fibrosis, Tay-Sachs disease, sickle cell anemia).

Somatic cells: Any cells in the body except reproductive cells and their precursors.

Southern blot: The nylon membrane to which DNA has adhered after the process of Southern blotting.

Southern blotting: The technique for transferring DNA fragments separated by electrophoresis from the gel to a nylon membrane, to which DNA probes that detect specific fragments can then be applied.

Specificity: The ability of a test to identify correctly those who do not have the characteristic which is being tested.

Stigmatization: Branding, marking, or discrediting because of a particular characteristic,

Sweat test: An assay used to confirm CF that measures levels of sodium (Na^+) and chloride (Cl-) ions. These ions appear in high concentrations in patients with CF. Sweating is induced by running a low electric current through a pilocarpine-soaked gauze pad on the individual's arm or back. The amounts of Na^+ and Cl^- in the sweat can then be determined to confirm or question a diagnosis of CF.

Tag **polymerase:** DNA polymerase-the enzyme used to form double-stranded DNA from nucleotides and a single-stranded DNA template—isolated from the bacterium *Thermus aquaticus,* which normally lives in hot springs, *Taq* polymerase can withstand the high temperatures required in the repeating cycles of polymerase chain reaction (PCR).

Tay-Sachs disease: A lethal autosomal recessive disorder affecting the central nervous system which results in mental retardation and early death. Tay-Sachs disease predominantly occurs among Jews of Eastern and Central European descent and populations in the United States and Canada descended from French Canadian ancestors.

Transcription: The synthesis of mRNA from a sequence of DNA (a gene); the first step in gene expression. Compare *translation.*

Translation: The process in which the genetic code carried by mRNA directs the synthesis of proteins from amino acids. Compare *transcription.*

Underwrite: The process by which an insurer determines whether and on what basis it will accept an application for insurance.

Wrongful birth: A malpractice claim in which the parents assert that failure to receive timely, accurate information robbed them of the opportunity to avoid conception or birth of an affected child.

Wrongful life: A malpractice claim in which an affected child asserts he or she was harmed by a failure to give the parents an opportunity to avoid conception or birth. The claimant argues that to never have existed would be better than to exist with severe disabilities.