

EXHIBIT 4

GLOSSARY OF TERMS.¹

<u>Term</u>	<u>Definition</u>
A&A TBG	<u>See</u> “Arthritis and Analgesia Therapeutic Business Group”
Abstract	Summary of a scientific study’s findings or of a published journal article.
Academic and Professional Affairs	At Merck, Subdivision of Medical and Scientific Affairs Department that administered the Continuing Medical Education program.
Acetaminophen	Pain reliever and fever reducer developed by McNeil Consumer Products under the brand name Tylenol (now available generically).
ACR	<u>See</u> “American College of Rheumatology”
ACRs	<u>See</u> “Acute Care Representatives”
ACS	<u>See</u> “Acute Coronary Syndrome”
Acute Care Representatives (ACRs)	Merck sales representatives who targeted healthcare professionals in hospitals.
Acute Coronary Syndrome (ACS)	Umbrella term covering a variety of conditions, all characterized by symptoms relating to a decrease in blood supply to the heart (<u>e.g.</u> , chest pains).
Acute myocardial infarction (AMI)	Sudden myocardial infarction; <u>see also</u> “Myocardial infarction”

¹ Some definitions used in this glossary are substantially similar to ones given in two sources. In those instances, the source is identified by a notation in parentheses following the definition. The notation (1) refers to Day*, S. Dictionary for Clinical Trials. West Sussex, England: John Wiley & Sons; 1999. The notation (2) refers to Thomas*, CL, ed. Taber’s Cyclopedic Medical Dictionary. Philadelphia, PA: F.A. Davis Co.; 1997.

<u>Term</u>	<u>Definition</u>
AD	See “ Alzheimer’s disease ”
Adenomatous colon polyps	Benign neoplastic tissue originating in the glandular epithelium of the colon. (2)
Adenosine diphosphate receptor antagonist	Antiplatelet agent that blocks adenosine diphosphate from binding to its receptor site on platelets and thereby decreases platelet activation and aggregation.
Adjudication	In the context of a clinical trial, the process through which investigator-reported adverse events are re-evaluated by a blinded independent panel according to pre-specified criteria to yield more accurate and consistent diagnoses.
ADVANTAGE	<u>Assessment of Differences Between Vioxx and Naproxen to Ascertain Gastrointestinal Tolerability and Effectiveness.</u> — Double-blind 12-week clinical trial conducted by the Clinical Development Program to assess the comparative gastrointestinal tolerability of Vioxx and naproxen.
Adverse event (AE)	Injury suffered by a patient while on a drug treatment that may or may not be caused by the treatment.
Advisory board	As used in this Report, any of a number of groups of 10 to 15 physicians with whom Merck’s Marketing Department met to discuss data from the Vioxx clinical program; the boards could include physicians with a shared specialty or could be multidisciplinary.
Advisory Committee	Committee of independent physicians that advises the FDA on matters within a defined medical area.
AE	See “ Adverse event ”
AERT	See “ Vioxx Adverse Experience Review Team ”
African green monkey (AGM) study	A Merck study conducted in African green monkey species to study the thrombotic effect of several drugs (including naproxen and Vioxx).

<u>Term</u>	<u>Definition</u>
Aggrastat	Merck drug (tirofiban hydrochloride injection) that inhibits platelet aggregation.
Alzheimer's disease (AD)	A chronic, progressive disorder that accounts for more than 50% of all dementias. (2)
American College of Rheumatology (ACR)	Professional organization of rheumatologists and associated healthcare providers that hosts an annual scientific meeting and publishes several peer-reviewed journals, including <u>Arthritis and Rheumatism</u> .
AMI	<u>See "Acute myocardial infarction"</u>
Analgesia	Absence of a normal sense of pain. (2)
Analgesic	A drug that relieves pain – e.g., NSAIDs.
Angina pectoris	Severe pain around the heart resulting from inadequate delivery of oxygen to the heart. (2)
Angioplasty	Alteration of a blood vessel, either surgically or by dilating the vessel using a balloon inside the lumen. (2)
Anticoagulant	An agent that prevents or delays the process of blood clot formation. (2)
Antiphospholipid syndrome	A disorder affecting coagulation due to the abnormal production of antibodies against cell membrane constituents and characterized by a tendency to develop thromboses.
Antiplatelet	Substance that interferes with platelet activity.
Antiplatelet Trialists Collaborative (APTC) composite cardiovascular endpoint	A composite cardiovascular endpoint, commonly used in clinical trials of antiplatelet agents, that includes all cardiac death, non-fatal myocardial infarction, and stroke (including both thrombotic and hemorrhagic strokes, and deaths with an unknown cause); <u>see also "Endpoint."</u>

<u>Term</u>	<u>Definition</u>
Antithrombotic	Preventing or interfering with thrombosis or blood coagulation. (2)
Approvable letter	In the context of a New Drug Application or supplemental New Drug Application, a letter sent by the FDA to the applicant indicating that the new indication and/or label changes requested are “approvable” subject to the submission of additional data.
APPROVe	<u>Adenomatous Polyp Prevention On Vioxx.</u> Placebo-controlled study of the efficacy of Vioxx in preventing adenomas in patients with a history of colorectal adenomas; also called Protocol 122; one of three cancer studies included in Protocol 203. After the External Safety Monitoring Board recommended stopping the trial on the basis of cardiovascular data, MRL discontinued the study and recommended voluntary withdrawal of Vioxx.
APTC composite cardiovascular endpoint	See “ <u>Antiplatelet Trialists Collaborative composite cardiovascular endpoint</u> ”
APTC event	Any cardiovascular adverse event that is among those included in the APTC composite cardiovascular endpoint.
Arachidonic acid	An essential fatty acid formed from unsaturated acids of plants and present in, for example, peanuts; a precursor of prostaglandins. (2)
Arcoxia	Merck’s second-generation selective Cox-2 inhibitor, approved by regulatory agencies in several foreign countries, but not marketed to date in the United States.
Arteriosclerosis	A disease of the arterial vessels marked by thickening, hardening, and loss of elasticity in the arterial walls, which may affect the functions of tissues and organs. (2)

<u>Term</u>	<u>Definition</u>
Arthritis	Inflammation of a joint, usually accompanied by pain, swelling, and, frequently, changes in structure. (2)
Arthritis and Analgesia Franchise Business Group	<u>See</u> “ Arthritis and Analgesia Therapeutic Business Group ”
Arthritis and Analgesia Therapeutic Business Group (A&A TBG)	Subdivision of Merck’s Marketing Department that developed marketing strategies and messages for Vioxx; later known as the “Arthritis and Analgesia Franchise Business Group.”
ASA	<u>See</u> “ Aspirin ”
Aspirin (ASA)	Non-selective NSAID that is a potent inhibitor of Cox-1 and is associated with cardioprotection.
Aspirin-indicated subgroup analysis	MRL post-hoc analysis of cardiovascular data from the VIGOR Trial that compared the number of cardiovascular events occurring among patients for whom aspirin prophylaxis was indicated (according to FDA criteria) with those for whom it was not; the analysis suggested that patients for whom aspirin prophylaxis was indicated suffered a disproportionate number of the cardiovascular adverse events in the study.
Association	A means by which two items are linked. For example, a link between an exposure (such as to a drug) and an outcome.
Atherogenesis	Formation of atheroma in the walls of the arteries. (2)
Atheroma	Collection of fatty plaque in the arteries.
Atherosclerosis	The most common form of arteriosclerosis, marked by cholesterol-lipid-calcium deposits in arterial linings. (2)
BARDS	<u>See</u> “ Biostatistics and Research Development Sciences ”
Bextra	Pfizer’s second-generation selective Cox-2 inhibitor.

<u>Term</u>	<u>Definition</u>
Bias	The systematic over- or under-estimation of a parameter, usually unknowingly and unintentionally.
Biostatistics	The application of statistical theory and methods in the biological and medical sciences. (1)
Biostatistics and Research Development Sciences (BARDS)	Subdivision of MRL that provided statistical support to Merck's clinical researchers.
Biosynthesis	The formation of chemical compounds by a living organism. (2)
BMS	<u>See</u> " Bristol-Myers Squibb "
Board of Scientific Advisors (BSA)	At Merck, a group of approximately eighteen prominent outside scientists who met annually to provide advice to MRL on issues regarding its clinical development programs.
Bristol-Myers Squibb (BMS)	A worldwide manufacturer of pharmaceuticals.
BSA	<u>See</u> " Board of Scientific Advisors "
Bulletins	Within Merck's United States Human Health division, internal communications between Merck's Marketing and Sales Departments drafted by the Market Integration Team and used to implement marketing strategies.
CABG	<u>See</u> " Coronary artery bypass grafting "
Cardiac prophylaxis	<u>See</u> " Cardiovascular prophylaxis "
Cardioprotection	An antithrombotic effect.
Cardiovascular (CV)	Pertaining to the heart and blood vessels. (2)

<u>Term</u>	<u>Definition</u>
Cerebrovascular accident (CVA)	Also known as a stroke; a sudden loss of consciousness followed by paralysis, caused by one of several different mechanisms including hemorrhage into the brain; formation of an embolus or thrombus that occludes an artery; or rupture of an extracerebral artery causing subarachnoid hemorrhage. (2)
Cardiovascular Adjudication SOP	<u>See</u> “ Cardiovascular Adjudication Standard Operating Procedure ”
Cardiovascular Adjudication Standard Operating Procedure (SOP)	As used in this Report, Merck’s standardized procedure for the collection and adjudication of cardiovascular adverse events occurring in clinical trials in Merck’s selective Cox-2 inhibitor program.
Cardiovascular Card	Promotional item for Vioxx containing a summary of cardiovascular data from the Phase IIb/III studies of Vioxx in an osteoarthritis patient population.
Cardiovascular prophylaxis	A treatment intended to prevent the occurrence of cardiovascular events – <u>e.g.</u> , a regimen of low-dose aspirin.
Case-control study	A type of epidemiological study used for evaluating the causes of a particular disease. A group of patients with a disease (the cases) are compared with another group of subjects who do not have the disease (the controls). Their lifestyles, previous exposure to potential hazards, demographics, etc., are compared to try to distinguish which of those features predisposes a patient to have the disease in question. (1)
Causal relationship	A relationship that is observed when one variable is a consequence of another. (1)
CBARDS	<u>See</u> “ Clinical Biostatistics and Research Decision Sciences ”
CBE	<u>See</u> “ Change Being Effected ”
CDER	<u>See</u> “ Center for Drug Evaluation and Research ”

<u>Term</u>	<u>Definition</u>
CDOC	<u>See</u> “ Clinical Development Oversight Committee ”
CDP	<u>See</u> “ Clinical Development Program ”
Celebrex	Selective Cox-2 inhibitor developed and marketed by Searle/Pfizer.
Celecoxib	Scientific name for Celebrex.
Center for Drug Evaluation and Research (CDER)	Division of the Food and Drug Administration responsible for ensuring that all over-the-counter and prescription drugs are safe and effective.
CFT	<u>See</u> “ Core Franchise Team ”
Change Being Effectuated (CBE)	Mechanism by which a pharmaceutical company can simultaneously change the label of a marketed product and submit the supplemental New Drug Application seeking approval for the change to the FDA for review and approval.
CHD	<u>See</u> “ Coronary heart disease ”
CHF	<u>See</u> “ Congestive heart failure ”
Class effect	Effect shared by related or similar drugs that is not specific to any particular molecule of the class.
CLASS Study	<u>Celecoxib Arthritis Safety Study</u> – Searle/Pfizer-sponsored study to assess the gastrointestinal safety of Celebrex relative to diclofenac and ibuprofen.
Clinical Biostatistics and Research Decision Sciences (CBARDS)	Subdivision of BARDS that provided statistical support to clinical researchers and created data analysis plans for clinical trials.
Clinical Development Oversight Committee (CDOC)	Merck committee that reviewed clinical development strategies and plans from a safety compliance and quality assurance perspective and determined whether and how study protocols should proceed; later known as “Clinical and Regulatory Review Committee” and currently the “Late Development Review Committee.”

<u>Term</u>	<u>Definition</u>
Clinical Development Program (CDP)	Subdivision of Merck’s Medical and Scientific Affairs Department that designed, implemented, and published post-marketing studies on the Company’s products, including Vioxx.
Clinical investigator	A doctor who sees patients in a clinical trial, oversees any interventions, such as drug administration, and records outcomes.
Clinical monitor	At Merck, an in-house scientist responsible for all medical aspects of a clinical trial, including the medical aspects of designing the trial and interpreting the results.
Clinical and Regulatory Review Committee (CRRC)	See “ Clinical Development Oversight Committee ”
Clinical Sciences	Subdivision of MRL responsible for the development, design, and implementation of clinical studies.
Clinical Study Report (CSR)	Document detailing the procedures and results of a clinical trial prepared by the company sponsoring the trial and submitted to the FDA.
Clinical trial or study	Study conducted in human beings for the purpose of determining a drug’s safety and/or efficacy for a particular use.
Clopidogrel	A potent oral antiplatelet agent marketed by Bristol-Myers Squibb and Sanofi-Aventis under the trade name Plavix.
CME	See “ Continuing Medical Education ”
Cohort study	The study of a group of subjects over time.
Colocalization	Presence of two or more objects or substances in a limited defined area.

<u>Term</u>	<u>Definition</u>
Combination therapy	As used in this Report, any of several proposed combinations in a single pill or capsule of Vioxx and an antiplatelet (e.g., aspirin, clopidogrel) or gastroprotective agent for the purpose of adding or allowing patients to add cardioprotection to Vioxx without compromising its gastroprotective qualities.
Comorbidity	The presence of one or more diseases or conditions in addition to the disease of interest in a clinical trial.
Comparator	The drug, placebo, or treatment (or other medical intervention) to which a new or experimental drug is being compared in the context of a clinical trial. (1)
Complicated PUBs	Gastrointestinal perforations, obstructions, and complicated upper-gastrointestinal bleeds; the secondary endpoint in the VIGOR Trial. Also known in this Report as “ Perforations, obstructions, and bleeds ” or “ POBs .”
Confidence interval	A range of values likely to encompass the true magnitude of a studied effect. A 95% confidence interval means that the statistical methodology used to perform the calculation at issue can be expected, 95 times out of 100, to generate a range of values that encompasses the true magnitude of the effect being measured.
Confounding variable	A variable, other than the variable of primary interest, that may affect the outcome measure in the course of a trial and that may or may not be known to investigators. (1)
Congestive heart failure (CHF)	Condition characterized by weakness, breathlessness, abdominal discomfort, and edema in the lower portions of the body resulting from venous stasis and reduced outflow of blood from the left side of the heart. (2)

<u>Term</u>	<u>Definition</u>
Consultants' Meeting	At Merck, a meeting of outside experts hosted by MRL to seek advice about particular scientific issues or by the Marketing Department to obtain market research.
Continuing Medical Education (CME)	Programs designed to provide ongoing medical education to physicians and through which physicians maintain their certification by accumulating credits from attendance at such lectures.
Coronary artery bypass grafting (CABG)	Surgical procedure by which narrowed arteries in the heart are bypassed with veins or arteries from outside the heart.
Coronary heart disease (CHD)	See "Ischemic heart disease"
Cosopt	Merck drug (dorzolamide hydrochloride-timolol maleate ophthalmic solution) for treatment of elevated intraocular pressure in patients with glaucoma.
Cox proportional hazards model	A statistical method for comparing the survival times between two or more groups of subjects that allows for adjustment for covariates and assumes a constant hazard rate over time. (1) One of the applications of the model is to test whether the hazard rates are proportional over time. The test produces a p-value indicating the strength of the evidence in favor of rejecting the model's assumption of constant hazards.
Cox-1	Enzyme that plays a role in protecting the lining of the stomach and mediates the production of certain prostaglandins, including thromboxane and perhaps also prostacyclin.
Cox-2	Enzyme responsible for causing pain and inflammation and mediating the production of certain prostaglandins, including prostacyclin and perhaps also thromboxane.

<u>Term</u>	<u>Definition</u>
Cox-2 hypothesis	Hypothesis underlying the development of selective Cox-2 inhibitors, including Vioxx, which posited that selective inhibition of the Cox-2 enzyme without inhibition of the Cox-1 enzyme would relieve pain and inflammation without causing gastrointestinal injury.
Coxib Task Force	At MRL, team created by Dr. Peter Kim in early 2001 to study the cardiovascular effects of Vioxx and Arcoxia.
Cozaar	Merck drug (losartan potassium) to reduce the risk of stroke in certain patients.
C-reactive protein (CRP)	A globulin that, in the presence of calcium ions, precipitates the C substance of pneumococcal cells. It is present in increased concentrations in the blood during the active phase of many inflammatory diseases. It is a marker of inflammation. (2)
Creatinine concentrations	Indicator of renal function.
Crixivan	Merck drug (indinavir sulfate) to be used in combination with other antiretroviral agents for the treatment of HIV infection.
Cross-sectional study	A study that examines all data at one particular point in time and does not consider within subject effects (<u>i.e.</u> , changes from the baseline). (1)
CRP	<u>See</u> “ C-Reactive Protein ”
CRRC	<u>See</u> “ Clinical and Regulatory Review Committee ”
Crude event rate	In the context of a clinical trial, the rate of events per patient without regard to the patients’ length of treatment.
CSR	<u>See</u> “ Clinical Study Report ”
CV	<u>See</u> “ Cardiovascular ”
CVA	<u>See</u> “ Cerebrovascular accident ”

<u>Term</u>	<u>Definition</u>
Cyclooxygenase	Endogenous enzyme that mediates the production of prostaglandins, including thromboxane and prostacyclin.
DAAODP	<u>See</u> “ Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products ”
DAP	<u>See</u> “ Data analysis plan ”
Data analysis plan (DAP)	Merck term for a pre-specified statistical methodology for interpreting raw data generated by a clinical or pre-clinical trial; also sometimes referred to as a “statistical data analysis plan” (SDAP).
Data dredging	Analyzing data without regard to accepted scientific and statistical principles in order to find some aspect that will be of interest. (1)
Data Safety Monitoring Board (DSMB)	In the context of a clinical trial, a group of individuals, who are unaffiliated with the sponsoring company, with relevant expertise (generally physicians and biostatisticians) responsible for reviewing unblinded or partially unblinded interim study data to ensure patient safety; also known as an “External Safety Monitoring Board” (ESMB).
DDMAC	<u>See</u> “ Division of Drug Marketing, Advertising and Communications ”
DDW	<u>See</u> “ Digestive Disease Week ”
Detail	In the context of pharmaceutical sales, a visit from a pharmaceutical sales representative to a doctor.
Detail aid	In the context of pharmaceutical sales, product pamphlet containing a drug’s labeling information used by pharmaceutical sales representatives in conversations with doctors.
Diclofenac	A non-selective NSAID developed by Ciba under the brand name Voltaren (now available generically).

<u>Term</u>	<u>Definition</u>
Digestive Disease Week (DDW)	Annual medical conference on gastrointestinal diseases.
Direct-to-consumer advertising (DTC)	Advertising directed at the general public, including television and magazine ads.
Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products (DAAODP)	Subdivision of the FDA's Center for Drug Evaluation and Research responsible for regulating the class of drugs to which Vioxx belongs. The division was responsible for reviewing the supplemental New Drug Application that Merck submitted following the VIGOR Trial.
Division of Drug Marketing, Advertising and Communications (DDMAC)	Subdivision of the FDA's Center for Drug Evaluation and Research that reviews prescription drug advertisements and promotional pieces; empowered to issue Warning Letters regarding such materials or refer issues regarding such materials to the FDA's legal division for possible enforcement action.
Dosage creep	As used in this Report, a phenomenon whereby patients consume higher than prescribed doses of a medication over time under the potentially mistaken belief that the higher doses will be more efficacious.
Dose response relationship	How the effect of a drug changes with dose. (1)
Dose-ranging study	Cinical trial to determine the effective dose of a medication for a specific indication.
Double-blind trial	Clinical trial in which both the patients and the investigators are ignorant (or "blinded") throughout the course of the trial as to whether any individual patient is receiving the study drug or a comparator.
DSMB	<u>See</u> " Data Safety Monitoring Board "
DTC	<u>See</u> " Direct-to-consumer advertising "
Dual-Cox inhibitors	NSAIDs that inhibit both Cox-1 and Cox-2; also called non-selective NSAIDs.

<u>Term</u>	<u>Definition</u>
Duration-effect	Effect of drug treatment that varies depending on the length of treatment.
Dyspepsia	Imperfect or painful digestion that is not a disease itself, but is symptomatic of a disease. (2)
Edema	A local or generalized condition in which the body tissues contain an excessive amount of tissue fluid. (2)
EDGE Trial	<u>E</u>toricoxib <u>D</u>iclofenac <u>G</u>astrointestinal <u>E</u>valuation. A one-year study by MRL comparing Arcoxia to diclofenac in osteoarthritis patients; a second trial using the same design, known as the EDGE II Trial, is currently in progress.
Educational Program Integration (EPI)	See “ Health Education Liaison ”
Endogenous	Produced or originating from within a cell or organism. (2)
Endoscopy study	A clinical trial in which an instrument known as an endoscope is used to examine the stomach lining and/or gastrointestinal tract for the presence of endoscopically detectable gastrointestinal injuries.
Endothelium	Layer of cells that lines many areas of the body, including the cavities of the heart and blood vessels.
Endpoint	A variable, which may relate to efficacy or safety, that is one of the primary interests in a study. (1)
Enteric aspirin	Aspirin tablet with a special coating that protects the stomach.
Enzyme	Protein molecule produced by living organisms that catalyses chemical reactions of other substances without itself being destroyed or altered upon completion of the reactions.
EPI	See “ Educational Program Integration ”

<u>Term</u>	<u>Definition</u>
Epidemiology	The study of health and disease in populations, including etiology, natural course, and treatments through the collection and analysis of statistical data concerning exposures to potential and known risk factors for diseases.
Epidemiology Department	Subdivision of Merck’s Biostatistics and Research Science Development Department that drafted data analysis plans for epidemiological studies and coordinated the adjudication of cardiovascular events.
ESMB	<u>See “External Safety Monitoring Board”</u>
Etodolac	A traditional non-selective NSAID developed by American Home Products under the brand name Lodine XL (now available generically).
Etoricoxib	Scientific name for Arcoxia .
EULAR	<u>See “European League Against Rheumatism”</u>
European League Against Rheumatism (EULAR)	British professional association for rheumatologists that hosts an annual scientific meeting.
Ex vivo	Outside of the living body; generally used to describe the study outside of the body of that which normally exists inside the body – e.g., drawn blood.
Exogenous	Originating outside an organ or part. (2)
Expedited review	In the context of FDA submissions, a procedure through which the FDA approves New Drug Applications and/or supplemental New Drug Applications on an abbreviated review schedule due to a demonstrable need for the treatment.
External Safety Monitoring Board (ESMB)	<u>See “Data Safety Monitoring Board”</u>
Exxpert	Rebate and educational program for Vioxx consumers.
FDA	<u>See “Food and Drug Administration”</u>

<u>Term</u>	<u>Definition</u>
Field Implementation Team (FIT)	Merck cross-functional team that coordinated the implementation of marketing strategies through the Company's sales force; formerly known as the Market Integration Team.
First patient in (FPI)	Date on which the first patient enters a clinical trial.
FIT	See " Field Implementation Team "
FitzGerald prostacyclin hypothesis	Hypothesis generated by Dr. Garret FitzGerald in 1997 that selective Cox-2 inhibitors might increase the risk of thrombotic cardiovascular events, based on his assumption that selective Cox-2 inhibitors suppressed vascular synthesis of prostacyclin (an antiplatelet agent and vasodilator) without concurrent suppression of thromboxane (known to induce platelet aggregation and vasoconstriction).
Flurbiprofen	A non-selective NSAID developed by Upjohn under the brand name Ansaid (now available generically).
Food and Drug Administration (FDA)	Federal agency within the Department of Health and Human Services responsible for regulating pharmaceutical products (among other things) in the United States.
Food, Drug, and Cosmetic Act	The federal statute that created the FDA and gives it the authority to regulate, among other things, pharmaceuticals.
Fosamax	Merck drug (alendronate sodium) for the treatment and prevention of osteoporosis.
FPI	See " First patient in "
Franchise Business Group	Subdivision of Merck's Marketing Department responsible for developing marketing strategies for a particular drug; formerly called Therapeutic Business Group.
Gastric mucosa	Layer of moist tissue that lines the stomach.

<u>Term</u>	<u>Definition</u>
Gastroenterologist	Physician specializing in the study of the physiology and pathology of the stomach, intestines, and related structures, such as the esophagus, liver, gallbladder, and pancreas. (2)
Gastrointestinal (GI)	Pertaining to the stomach and intestine. (2)
Generalizability	The extent to which conclusions (e.g., of a clinical trial) can be applied to a wide population. (1)
GI	See “ Gastrointestinal ”
GP IIb/IIIa receptor antagonist	Antiplatelet agent that operates by interrupting the final pathway of platelet aggregation, the binding of fibrinogen (or Von Willenbrand factor) to its platelet membrane GpIIb/IIIa receptor; identified in a 1998 Merck patent for potential combination with Vioxx or another selective Cox-2 inhibitor in a single pill.
Half-life	Time required by the body, tissue, or organ to metabolize or inactivate half the amount of a substance taken in. (2)
Hazard rate	Probability of a given event occurring at a particular point in time, given that the event has not yet occurred. (1)
Hazard ratio	Ratio of two hazard rates either at a particular point in time or averaged over a long period. (1)
Health Education Liasion (HEL)	Merck promotional program consisting of presentations by Merck personnel or other parties that educated doctors about the Company’s products, including Vioxx.
Health Science Associate (HSA)	Merck sales representatives specially trained to discuss scientific information concerning the Company’s products with thought leaders.
HEL	See “ Health Education Liaison ”
Hepatic	Pertaining to the liver. (2)

<u>Term</u>	<u>Definition</u>
Heterogeneous	Consisting of elements that are not of the same kind or nature.
HHPAC	<u>See</u> “ Human Health Product Approval Committee ”
Homeostasis	The state of dynamic equilibrium of the internal environment of the body that is maintained by the ever-changing processes of feedback and regulation in response to external or internal changes. (2)
Hormone	A substance originating in an organ, gland, or body part that is conveyed through the blood to another body part, chemically stimulating that part to increase or decrease functional activity or to increase or decrease secretion of another hormone. (2)
HSA	<u>See</u> “ Health Science Associate ”
Human Health Product Approval Committee (HHPAC)	Merck’s second-highest ranking cross-functional committee, including members of the Company’s Marketing, Research, and Manufacturing Departments.
Hypertension	A condition in which a patient has higher than normal blood pressure. (2)
Hypothesis	A tentative theory or postulated explanation of an observed phenomenon that may be a likely explanation, but requires further investigation for verification.
Hyzaar	Merck drug (losartan potassium-hydrochlorothiazide) for the treatment of hypertension.
Ibuprofen	A non-selective NSAID developed by The Boots Co. under the brand name Nurofen (now available generically). Current trade names include Motrin and Advil.
ICH	<u>See</u> “ International Committee on Harmonisation ”
IHD	<u>See</u> “ Ischemic heart disease ”

<u>Term</u>	<u>Definition</u>
In vitro	In the context of a scientific experiment or trial, pertaining to a test done in a test tube or other artificial environment (literally, within a glass) of a biological process or reaction that would normally occur in a human being or other organism.
In vivo	In the context of a scientific experiment or trial, pertaining to a test done inside a living body of a biological process or reaction.
Indication	Disease or condition for which the FDA has approved a treatment.
Indobufen	A non-selective NSAID.
Indomethacin	A non-selective NSAID developed by Merck under the brand name Indocid (now available generically).
Integrated Summary of Safety (ISS)	Section of New Drug Application that comprehensively analyzes safety data for the proposed drug.
Intention-to-treat (ITT) analysis	Strategy for analyzing study data, which says that any subject randomized to treatment must be followed throughout the intended treatment period included in the analysis, even if the subject discontinues the trial prematurely.
International Committee on Harmonisation (ICH)	Collaborative of regulatory agencies and pharmaceutical experts throughout the world dedicated to the improvement of the drug development process.
Interviewer bias	In a clinical trial including data collected by means of interviews with study participants, bias caused by the manner in which an interviewer elicited or recorded such information.
Ischemic heart disease (IHD)	A lack of oxygen supply to the heart, with consequent altered cardiac function. The most common cause of myocardial ischemia is atherosclerosis of the coronary arteries. Also known as “coronary heart disease.” (2)

<u>Term</u>	<u>Definition</u>
Isoform	A protein that serves a similar function to, but takes a slightly different form from, another protein.
ISS	<u>See</u> “ Integrated Summary of Safety ”
ITT	<u>See</u> “ Intention-to-treat analysis ”
JRA	<u>See</u> “ Juvenile rheumatoid arthritis ”
Juvenile rheumatoid arthritis (JRA)	Rheumatoid arthritis occurring in children.
Kaplan-Meier curve	A graph showing the cumulative incidence of an outcome of interest over time.
Knockout mice	Mice bred without a given gene or receptor for scientific purposes; as used in this Report, mice bred without prostacyclin receptors that Murata <i>et al.</i> studied to determine the effects of selectively and completely inhibiting prostacyclin.
Label	Complete prescribing information for a drug, including warnings and precautions developed by pharmaceutical companies in consultation with the FDA and approved by the FDA.
Large Simple Trial	A trial where treatment is administered in a naturalistic setting that is intended to mirror standard practice, and the outcomes measured are simple and available in the typical practice setting.
Last patient out (LPO)	Date on which last patient in a clinical trial completes his or her course of treatment.
Late Development Review Committee (LDRC)	<u>See</u> “ Clinical Development Oversight Committee ”
LDRC	<u>See</u> “ Late Development Review Committee ”

<u>Term</u>	<u>Definition</u>
Licensing Management Committee	Cross-functional Merck committee that met regularly to consider licensing the products of other companies; this committee considered licensing several products for use in combination with Vioxx. <u>See also</u> “ Combination therapy ”
Linear Time Test	As used in this Report, test of the proportional hazards assumption using the Cox proportional hazards model including terms for the main treatment effect and time*treatment .
log(time)*treatment	As stated in the published version of the APPROVe Trial article, interaction term included in the Cox proportional hazards model used to test the assumption of proportional hazards; a version of the model using the logarithm of time.
Logarithm of Time Test	As used in this Report, test of the proportional hazards assumption using the Cox proportional hazards model including terms for the main treatment effect and log(time)*treatment .
Low-dose aspirin	Daily dose of approximately 80 mg of aspirin taken for cardioprotection by patients at-risk for cardiovascular events.
LPO	<u>See</u> “ Last patient out ”
Lumiracoxib	Scientific name for Prexige .
Management Committee	Senior-most Merck Committee, comprising the Chief Executive Officer and his direct reports.
MAP	<u>See</u> “ Merck Adherence Program ”
Market Integration Team (MIT)	<u>See</u> “ Field Implementation Team ”
Marketing Services	Subdivision of Merck’s United States Human Health Division that implemented the strategies developed by the Company’s Marketing Department.

<u>Term</u>	<u>Definition</u>
Maxalt	Merck drug (rizatriptan benzoate) for the acute treatment of migraine attacks.
MEDAL Trial	<u>Multi-National Etoricoxib Diclofenac Arthritis Long-Term Trial</u> . An ongoing long-term clinical trial by MRL studying the cardiovascular effects of Arcoxia versus diclofenac in over 20,000 osteoarthritis patients.
Medical and Scientific Affairs (MEDSA)	Subdivision of Merck's United States Human Health Division that conducted scientific research and programs to support marketing and sales efforts.
Medical School Grant Program (MSGP)	Program through which Merck funded studies of Vioxx by unaffiliated researchers.
Medical Services	Subdivision of Merck's Medical and Scientific Affairs Department that responded to questions about Merck products from doctors and other health care providers.
Medical/Legal Review Board (MLRB)	Brand- or franchise-specific committee often including one lawyer, one clinical scientist or MEDSA physician, and one regulatory scientist that was responsible for ensuring Merck's promotional and other released materials concerning a particular drug or drugs complied with federal regulations and Company policies.
Medication compliance	Extent to which patients in a study followed a prescribed dosing regimen.
MEDSA	See " <u>Medical and Scientific Affairs</u> "
Merck Adherence Program (MAP)	Retention program for Vioxx.
Merck Frosst	Merck's basic research laboratory in Montreal, Canada. Merck Frosst specializes, among other things, in prostaglandin basic research.

<u>Term</u>	<u>Definition</u>
Merck Research Labs (MRL)	Division of Merck responsible for conducting clinical studies necessary to obtain regulatory approvals, specific labeling, and new indications.
Merck Sharpe & Dohme (MSD)	Name of Merck's European subsidiary.
Merlin	Computer program through which sales associates could access information about which drugs a physician prescribed.
Meta-analysis	A statistical procedure for combining results from a number of studies and investigations in order to analyze the therapeutic effectiveness of specific treatment and plan future studies. (2)
Metabolism	The sum of all physical and chemical changes that take place within an organism; all energy and material transformations that occur within living cells. (2)
Metabolite	A byproduct of metabolism detectible in bodily excretions and a potential indicator of the presence and quantity of the metabolized substance in the body.
MI	<u>See</u> " Myocardial infarction "
MIT	<u>See</u> " Market Integration Team "
MK-0663	Merck designation for the Arcoxia molecule.
MK-0966	Merck designation for the Vioxx molecule.
MLRB	<u>See</u> " Medical/Legal Review Board "
Mortality rate	In a clinical trial, the proportion of subjects who have died at any given point in time. (1)
MRL	<u>See</u> " Merck Research Laboratories "
MSD	<u>See</u> " Merck Sharpe & Dohme "
MSGP	<u>See</u> " Medical School Grant Program "

<u>Term</u>	<u>Definition</u>
MVX	Broadcast voicemail messages drafted by the Field Implementation Team and used by senior sales executives to communicate with the Merck's sales force.
Myocardial infarction (MI)	Term used to describe irreversible injury to the heart muscle; also known as "heart attack."
Nabumetone	A non-selective NSAID developed by SmithKline Beecham under the brand name Relafen (now available generically); used as a comparator drug in several Vioxx trials, including Protocols 085 and 090.
Naproxen	A non-selective NSAID developed by Syntex Laboratories, Inc. under the brand name Anaprox (now available generically). Naproxen is characterized by a long half-life and high degree of Cox-1 inhibition.
Naproxen cardioprotection hypothesis	As used in this Report, hypothesis advanced by MRL scientists in the aftermath of the VIGOR Trial that the non-selective NSAID naproxen, when taken in a sustained manner, provides cardioprotection through potent and long-lasting inhibition of Cox-1.
National Institutes of Health (NIH)	The primary federal agency (part of the U.S. Department of Health and Human Services) for conducting and supporting medical research.
NDA	<u>See "New Drug Application"</u>
NEJM	<u>See "New England Journal of Medicine"</u>
Nested case-control study	In epidemiology, case-control study performed in the course of a cohort study.
New Drug Application (NDA)	Application submitted to the FDA in support of a request for authorization to market a new drug in the United States for the treatment of a specified disease state or symptom in humans.

<u>Term</u>	<u>Definition</u>
New users	In epidemiology, members of a cohort who have not received a certain treatment within a specified period of time prior to the beginning of an observational study; <u>see also</u> “ Cohort study .”
NIH	<u>See</u> “ National Institutes of Health ”
Nitric oxide (NO)	Vasodilator that helps prevent gastrointestinal ulcers, which frequently are caused by constricted blood vessels in the stomach; considered by Merck for possible combination with Vioxx; <u>see also</u> “ Combination therapy .”
NO	<u>See</u> “ Nitric oxide ”
Nonparticipation bias	Bias caused by a potential study participant’s decision not to participate in a given study.
Non-steroidal anti-inflammatory drug (NSAID)	Any of a class of commonly used drugs that relieve pain and inflammation by inhibiting cyclooxygenase; examples include aspirin and ibuprofen (traditional NSAIDs that inhibit both Cox-1 and Cox-2), and Vioxx (which selectively inhibits Cox-2).
Nonselective NSAID	A non-steroidal anti-inflammatory drug that appreciably inhibits both Cox-1 and Cox-2.
Null hypothesis	The assumption that there is no difference between groups.
NSAID	<u>See</u> “ Non-steroidal anti-inflammatory drug ”
NSAID cardioprotection hypothesis	As used in this Report, hypothesis, articulated in a memorandum written by MRL’s Dr. Thomas Musliner in 1996, that NSAIDs other than aspirin may provide antiplatelet effects and resultant cardioprotection by inhibiting Cox-1.
NSAID GI warning	FDA-mandated Warning in the label of all NSAIDs indicating that this class of drugs may cause gastrointestinal adverse events.

<u>Term</u>	<u>Definition</u>
OA	<u>See</u> “ Osteoarthritis ”
Observational study	A study that has no experimental intervention, but rather evaluates a hypothesis through the collection and analysis of existing statistical data; <u>see also</u> “ Epidemiology .”
Obstacle handlers	Scripts prepared by the Arthritis and Analgesia Therapeutic Business Group and the Marketing Integration Team for use by the sales representatives in responding to questions by physicians about a drug that relate to safety or other concerns.
Obstacles	As used in this Report, pharmaceutical industry term for questions about a drug that relate to safety or other concerns that arise in the context of a conversation between a sales representative and physician.
Odds	The probability of an event’s occurring divided by the probability of it not occurring. (1)
Odds ratio (OR)	The ratio of two odds, often used as a summary of the size of a treatment effect. <u>See</u> “ Odds ” (1)
Off-drug analysis	A statistical analysis of outcomes occurring after the patients in a clinical trial have ceased treatment.
Office of Medical/Legal (OML)	Subdivision of Merck’s Marketing Services Department responsible for communicating with the FDA’s Division of Drug Marketing, Advertising, and Communications and coordinating meetings of the Medical/Legal Review Boards.
OML	<u>See</u> “ Office of Medical/Legal ”
On-drug analysis	A statistical analysis of outcomes occurring during or close to the time that patients in a clinical trial are receiving treatment.
Once daily dosing	Type of regimen in which a patient must take only one dose of a medication each day.

<u>Term</u>	<u>Definition</u>
OR	<u>See</u> “ Odds ratio ”
Osteoarthritis (OA)	A type of arthritis marked by progressive cartilage deterioration in synovial joints and vertebrae and, potentially, overgrowth of bony tissue beyond the joint margins.
Outcome	<u>See</u> “ Endpoint ”
Outcomes Research	At Merck, Subdivision of Medical and Scientific Affairs Department that studied health care policy issues.
Outlier	In the context of a scientific experiment or study, a data value that does not seem to be true, given all the other data values, usually because it is very extreme (either too large or too small). (1)
Oxaprozin	A non-selective NSAID developed by Searle under the brand name Daypro (now available generically).
Package insert	<u>See</u> “ Label ”
Parecoxib	Intravenous version of valdecoxib (Bextra), a selective Cox-2 inhibitor produced by Pfizer.
Patent and Trademark Office (PTO)	A federal agency within the U.S. Department of Commerce that secures to inventors, for a limited time, the right to exclusive use of their inventions.
Patient years at risk (PYR)	In the context of a clinical trial, measure of total time that patients enrolled in the trial collectively were on a given treatment, calculated by summing the duration of each particular patient’s period of treatment.
Percutaneous transcatheter angioplasty (PTCA)	Catheter-based procedure used to widen narrowed coronary arteries.
Perforations, ulcers, and bleeds (PUBs)	As used in this Report, types of gastrointestinal complications traditionally associated with NSAID use; primary endpoint in the VIGOR Trial.

<u>Term</u>	<u>Definition</u>
Perforations, obstructions, and Bleeds	Gastrointestinal perforations, obstructions, and complicated upper-gastrointestinal bleeds; the secondary endpoint in the VIGOR Trial. Also known in this Report as “ Complicated PUBs ” or “ POBs ”
Periodic Safety Update Report (PSUR)	Report containing safety data on marketed pharmaceuticals submitted by drug-makers to the FDA and foreign regulatory agencies every six months.
Peripheral edema	Edema in the extremities (e.g., the hands or feet), which causes swelling of the extremities.
PGI2	<u>See</u> “ Prostacyclin ”
PGI-M	Prostacyclin metabolite measurable in the urine and hypothesized to reflect the body’s production of prostacyclin.
Pharmacoepidemiology	The study of drug usage and results (positive and negative) in broad populations with a view to a better understanding of beneficial drug usage. (1)
Pharmacology	The study of drugs (including uses, benefits, harmful effects, and stability). (1)
Phase I study	In the FDA-regulated drug development process, the earliest types of studies that are carried out in humans, typically done using small numbers (often less than 20) of healthy subjects and are to investigate toxicity, as well as the action of the drug on the physiology of the body and the action of the body on the drug. (1)
Phase II study	Clinical trials carried out in patients, rather than healthy subjects, usually to find the best dose of the drug and to investigate safety and efficacy.
Phase III study	Generally, major clinical trials aimed at conclusively demonstrating the safety and efficacy of a drug for a particular use. (1)

<u>Term</u>	<u>Definition</u>
Phase IV/V study	Clinical trials carried out after a drug receives approval from the FDA; often conducted for marketing purposes as well as to gain broader experience with the new product. (1)
Physician Information Request (PIR)	As used at Merck, physician questions relayed by sales representatives to Medical and Scientific Affairs for response, typically pertaining to off-label information which the sales representatives were not permitted to discuss.
Pill-splitting	Practice of dividing a pill into halves and taking the divided doses.
Pilot study	A small study for help in designing a further, confirmatory study. (1)
Pipeline	In the pharmaceutical industry, a term referring to the products under development that may be marketable in the foreseeable future.
PIR	<u>See</u> “ Physician Information Request ”
Placebo	Inert treatment administered to a control group in a clinical trial to establish a baseline against which effects of any drug under study may be evaluated.
Plaque	As used in this Report, a yellow swollen area of the lining of an artery, formed by the accumulation of lipids and inflammatory cells in arterial walls. (2)
Platelets	Microscopic round or oval disks found in the blood of human beings that play an important role in blood coagulation, hemostasis, and blood thrombus formation. (2)
PN	<u>See</u> “ Protocol number ”
POBs	<u>See</u> “ Complicated PUBs ” and “ Perforations, obstructions, and bleeds ”

<u>Term</u>	<u>Definition</u>
Policy letters	As used in this Report, memoranda issued to Merck sales representatives outlining Company policies governing the content of communications between representatives and physicians and related matters.
Pooled analysis	Analysis of combined patient-level data drawn from different studies.
Positive predictive value	In a diagnostic test, the probability that a person with a positive result does actually have the disease (<u>i.e.</u> , that the result is correct). (1)
Post-ACS	Condition of having suffered one of the diseases included with the category of Acute Coronary Syndrome.
Post hoc analysis	Any analysis of clinical trial data conceived with knowledge of other results of a clinical trial.
Poster	As used in this Report, summary from clinical trials or other scientific studies presented at conferences.
PPI	<u>See</u> “ Proton Pump Inhibitor ”
Prexige	Selective Cox-2 inhibitor developed and marketed by Novartis.
Primary dysmenorrhea	Pain associated with menstruation that is not caused by a known pathological condition. (2)
Product circular	<u>See</u> “ Label ”
Professional Information Request	<u>See</u> “ Physician Information Request ”
Propecia	<u>See</u> “ Proscar ”
Proscar	Merck drug (finasteride) for the treatment of male pattern hair loss; also known as “Propecia.”

<u>Term</u>	<u>Definition</u>
Prostacyclin (PGI₂)	A prostaglandin – existing in the vascular endothelium, kidney, lung and in other parts of the body – believed to be the most potent antiplatelet agent and a vasodilator.
Prostacyclin hypothesis	See “ FitzGerald prostacyclin hypothesis ”
Prostaglandin	Compound derived from arachidonic acid that mediates a variety of processes, including vasodilation and vasoconstriction (for example, prostacyclin).
Prostanoids	Collective term for prostaglandins and thromboxanes.
Prothrombotic	Tending to cause or increase the risk of thrombosis.
Protocol	As used in this Report, a written document describing all the important details of how a study will be conducted (including the products used, study rationale, procedures to be carried out on the subjects, number of subjects, and study design) and describing how the data will be analyzed. (1)
Protocol 010	Merck Phase IIa study comparing the effects of Vioxx 25 mg, Vioxx 125 mg, and placebo in osteoarthritis patients.
Protocol 023	Merck study of renal effects of Vioxx, which demonstrated that Vioxx was associated with a reduction in the prostacyclin urinary metabolite but not the thromboxane urinary metabolite, which suggested that some prostacyclin production may be mediated by Cox-2, and inspired the FitzGerald prostacyclin hypothesis.
Protocol 059	Proposed Merck “megatrial” of Vioxx versus ibuprofen and diclofenac intended to prove the Cox-2 hypothesis; cancelled before any patients were enrolled.
Protocol 061	Merck pharmacological study demonstrating that naproxen significantly impeded blood clotting in <u>ex vivo</u> assays.

<u>Term</u>	<u>Definition</u>
Protocol 068	A year-long Merck study comparing the efficacy of Vioxx 25 mg versus naproxen 1000 mg for the treatment of rheumatoid arthritis.
Protocol 069	Merck's pooled analysis of gastrointestinal safety outcomes from all Phase IIb/III Vioxx clinical trials in osteoarthritis patients.
Protocol 078	Merck placebo-controlled clinical trial of the efficacy of Vioxx 25 mg in preventing the onset of Alzheimer's disease.
Protocol 085	Three-arm, six-week study conducted by Merck's Clinical Development Program in osteoarthritis patients comparing Vioxx 12.5 mg, nabumetone, and placebo; twin study to Protocol 090.
Protocol 090	Three-arm, six-week study conducted by Merck's Clinical Development Program in osteoarthritis patients comparing Vioxx 12.5 mg, nabumetone, and placebo; twin study to Protocol 085.
Protocol 091	Merck placebo-controlled clinical trial of the efficacy of Vioxx 25 mg in slowing the progression of Alzheimer's disease.
Protocol 096	One of two studies comparing the use of Vioxx and naproxen for the treatment of rheumatoid arthritis that was ongoing at the time the results of the VIGOR Trial became available.
Protocol 097	One of two studies comparing the use of Vioxx and naproxen for the treatment of rheumatoid arthritis that was ongoing at the time the results of the VIGOR Trial became available.
Protocol 126	Merck placebo-controlled clinical trial of the efficacy of Vioxx in slowing the progression of Alzheimer's disease; cancelled after Protocol 091 demonstrated a lack of efficacy.

<u>Term</u>	<u>Definition</u>
Protocol 136	Merck three-arm endoscopy study comparing the effect on the stomach of (i) Vioxx 25 mg and aspirin; (ii) aspirin alone; and (iii) ibuprofen alone.
Protocol 158	Merck-planned two-arm endoscopy study comparing the effect on the stomach of (i) Vioxx 25 mg and aspirin and (ii) a non-selective NSAID and aspirin; cancelled in August 2003 before any patients enrolled.
Protocol 203	Merck cardiovascular outcomes study designed to pool and analyze cardiovascular event data from three ongoing or planned placebo-controlled trials of the efficacy of Vioxx in the treatment or prevention of various forms of cancer (Protocols 122, 145, and 201).
Protocol number (PN)	As used in this Report, a number assigned by Merck to a particular study.
Proton pump inhibitor (PPI)	A drug that blocks the production of stomach acid, and therefore is used to heal stomach and duodenal ulcers.
PSUR	<u>See</u> “ Periodic safety update report ”
PTCA	<u>See</u> “ Percutaneous transcatheter angioplasty ”
Public Affairs	Department of Merck that interacted with the media and developed press releases and other public statements about the Company and its products.
PUBs	<u>See</u> “ Perforations, ulcers, and bleeds ”
P-value	The probability of getting a result at least as extreme as that observed if the null hypothesis is true. (1) A p-value equal to or less than 0.05 is generally understood to mean that the result is statistically significant.
PYR	<u>See</u> “ Patient years at risk ”
RA	<u>See</u> “ Rheumatoid arthritis ”

<u>Term</u>	<u>Definition</u>
Randomized clinical trial (RCT)	A clinical trial in which patients are randomly assigned to different treatment groups, including a control group that serves as the basis for comparison with the treatment of interest.
RCT	<u>See</u> “ Randomized clinical trial ”
Regulatory Affairs	Subdivision of MRL responsible for developing and communicating MRL’s positions on regulatory issues to regulatory agencies, including the FDA.
Relative risk (RR)	Estimate of comparative risk, which is calculated by dividing the incidence rate for a given adverse event (<u>e.g.</u> , PUBs) in one group by the incidence rate or such events in another group.
Renal	Of or relating to the kidney.
Report Evaluation Safety Surveillance (RESS)	Subdivision of Merck’s Worldwide Product Safety and Epidemiology Department responsible for monitoring and evaluating post-marketing adverse event data to determine whether the data warranted a safety-related modification to the product label or a safety-related notification to healthcare professionals.
Reporting bias	In epidemiology, bias caused by a study participant’s failure to accurately report which drugs he or she has used or his or her risk factors for developing disease.
Reprints	As used in this Report, copies of published scientific articles distributed to physicians and/or used to educate representatives or other constituencies.
RESS	<u>See</u> “ Report Evaluation Safety Surveillance ”
Rheumatoid arthritis (RA)	A chronic systemic disease marked by inflammatory changes in joints and related structures that result in crippling deformities. (2)
Rheumatologist	Physician who specializes in acute or chronic diseases characterized by inflammation, muscle soreness and stiffness, and pain in joints and associated structures.

<u>Term</u>	<u>Definition</u>
Risk ratio (RR)	See “ Relative risk ”
Rofecoxib	Scientific name for Vioxx.
RR	See “ Risk ratio ” and “ Relative risk ”
SAE	See “ Serious adverse experience ”
Safety Update Report (SUR)	Periodic report containing detailed data on drug safety required by the FDA for all marketed drugs.
Sales Training and Professional Development (STPD)	At Merck, the unit within Sales Department that trained sales representatives.
SDAP	See “ Statistical data analysis plan ”
Secondary prophylaxis	Measures to prevent recurrence of a disease – e.g., daily treatment with low-dose aspirin to prevent successive cardiac events.
Selection bias	The bias caused by the fact that the types of subjects who take part in studies are not a random sample of the population from which they are drawn. (1)
Selective Cox-2 inhibitor	NSAID that selectively inhibits the Cox-2 enzyme, but only minimally inhibits the Cox-1 enzyme.
Serious adverse experience (SAE)	In the context of a clinical trial, a life-threatening adverse event, or one resulting in death, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.
Singulair	Merck drug (montelukast sodium) for the treatment of indoor and outdoor allergies.

<u>Term</u>	<u>Definition</u>
Site monitor	In a clinical trial, one who visits investigators to help with study management, ensures that all data are being recorded as they should be and that all supplies are available on site, and who often returns completed case record forms (including documentation of adverse events) to the data management office. (1)
sNDA	<u>See</u> “ Supplemental New Drug Application ”
SOP	<u>See</u> “ Standard operating procedure ”
Standard operating procedure (SOP)	As used in this Report, unified procedure for accomplishing a specific task adopted throughout Merck.
Statistical data analysis plan (SDAP)	<u>See</u> “ Data analysis plan ”
Statistical power	In statistical significance tests, the probability that the null hypothesis, which states that there is no difference between the groups being compared, will be rejected if it is not true. (1)
Statistical significance	The claim that is generally made when the calculated p-value from a statistical significance test is less than a prespecified significance level (often meaning $P < 0.05$) so that the null hypothesis can be rejected. (1)
Statistics	As used in this Report, the art, philosophy, and science of using statistical methods to design, manage, analyze and draw conclusions from studies. (1)
STPD	<u>See</u> “ Sales Training and Professional Development ”
Stroke	<u>See</u> “ Cerebrovascular accident ”
Subgroup analysis	An analysis of the results of a clinical trial with respect to a subsample of all randomized patients rather than all patients randomized. (1) This term may also refer to any analysis of a portion of a clinical trial dataset – e.g., for specific time intervals.

<u>Term</u>	<u>Definition</u>
SUCCESS VI & VII	Trials sponsored by Searle/Pfizer comparing the renal safety of Vioxx 25 mg and Celebrex 200 mg. Both studies concluded that Celebrex had the superior renal safety profile.
Supplemental New Drug Application (sNDA)	Submission of scientific data to the FDA in support of a change in a drug's labeling.
SUR	<u>See "Safety Update Report"</u>
Synthesis	As used in this Report, process by which constituent elements are combined to form a new substance.
Systemic lupus erythematosus	A chronic autoimmune inflammatory disease involving multiple organ systems and marked by periods of exacerbation and remission. (2)
Systemic prostacyclin	Prostacyclin synthesized in a part of the body other than the kidney.
Systolic blood pressure	Measure of blood pressure based on tension exerted by blood against the arterial walls during contraction of the ventricle.
TARGET	A Novartis trial to assess safety (including cardiovascular safety), tolerability, and efficacy of its selective Cox-2 inhibitor, Prexige, as compared to ibuprofen and naproxen.
TCE	<u>See "Thromboembolic cardiovascular event"</u>
Thromboembolic cardiovascular event (TCE)	A cardiovascular adverse event related to, caused by, or characterized by obstruction or occlusion of a vessel by a detached thrombus or blood clot; examples include: myocardial infarction, sudden death, or cerebrovascular event.
Thrombosis	The formation, development, or existence of a blood clot or thrombus within the vascular system. (2)

<u>Term</u>	<u>Definition</u>
Thrombotic event²	An adverse event related to, caused by, or characterized by formation or presence of a thrombus or blood clot; examples include: myocardial infarction, ischemic stroke, and venous events such as pulmonary embolism.
Thromboxane	An eicosanoid belonging to the group of prostanoids, biochemically related to the prostaglandins, that is synthesized by platelets and promotes platelet aggregation (i.e., coagulation) and vasoconstriction; its synthesis is mediated by predominantly the Cox-1 isoform, but some thromboxane appears to be Cox-2 dependent.
Thromboxane receptor antagonist (TRA)	Antiplatelet agent that functions by interfering with the binding of thromboxane to its receptor sites, thereby blocking platelet activation and aggregation.
Thromboxane synthase inhibitor (TSI)	Antiplatelet agent that impedes the formation of thromboxane and thereby decreases the total amount of thromboxane available to bind to its receptor sites, blocking platelet activation and aggregation.
TIA	<u>See “Transient ischemic attack”</u>
Time to occlusion (TTO)	Measure of the rate at which blood clots form and block a blood vessel.
time*treatment	Interaction covariate included in the Cox proportional hazards model used to test the assumption of proportional hazards in the published article on the APPROVe Trial; a version of the model using linear time.

² Some Merck documents refer to certain cardiovascular events as “thrombotic.” Other Merck documents refer to these same events as “thromboembolic.” Although there is a clinical difference, witnesses and Merck internal documents used these terms interchangeably to refer to cardiovascular events caused by a clot, such as a myocardial infarction or stroke, and we do not distinguish between them for purposes of this Report.

<u>Term</u>	<u>Definition</u>
Time-to-event plot	Plot of study data showing the cumulative number of events on different treatments at different stages over the course of a study.
Toxicity	The extent, quality, or degree of being poisonous. (2)
TRA	<u>See</u> “ Thromboxane Receptor Antagonist ”
Tramadol	Non-NSAID analgesic marketed by Ortho-McNeil Johnson & Johnson under the brand name Ultram (now available generically).
Transient ischemic attack (TIA)	Temporary interference with blood supply to the brain, with symptoms only lasting for a few moments or several hours and no remaining evidence of residual brain or neurological damage. (2)
TSI	<u>See</u> “ Thromboxane Synthase Inhibitor ”
TTO	<u>See</u> “ Time to occlusion ”
TX-M	Metabolite of thromboxane excreted from the body in urine; a potential indicator of the level of thromboxane in the body.
Tylenol	<u>See</u> “ Acetaminophen ”
UKGPD	<u>See</u> “ United Kingdom General Practitioner Database ”
Ultram	<u>See</u> “ Tramadol ”
Unblinding	Process through which clinical investigators become aware of the treatment assignments for individual patients.
United Kingdom General Practitioner Database (UKGPRD)	Healthcare database in the United Kingdom.

<u>Term</u>	<u>Definition</u>
United States Human Health (USHH)	Organization within Merck responsible for the domestic marketing and sales of the Company's products.
USHH	<u>See</u> " United States Human Health "
Valdecoxib	Scientific name for Bextra, a selective Cox-2 inhibitor developed and marketed by Pfizer.
VALOR	<u>Vioxx-Aspirin Long-term Outcomes Research</u> . Cardiovascular outcomes study of Vioxx plus aspirin versus aspirin alone to test the theory that the anti-inflammatory characteristic of Vioxx would confer a cardiovascular benefit in patients with a recent history of acute coronary syndromes; cancelled in March 2002 before any patients were enrolled.
Vasculature	The arrangement of blood vessels in the body or any part of it, including their relationship and functions. (2)
Vasoconstriction	Decrease in the diameter of a blood vessel that impairs blood flow through the vessel.
Vasodilation	Increase in the diameter of a blood vessel due to relaxation of the smooth muscle within the vessel wall that permits greater blood flow.
Vasodilator	Agent that causes dilation of the blood vessels.
VICTOR	<u>Vioxx in Colorectal Cancer Therapy Optimal Regime</u> . Placebo-controlled study by Oxford University of the efficacy of Vioxx in preventing colorectal cancer discontinued after the voluntary withdrawal of Vioxx in 2004; also known as Protocol 145. One of three studies that comprised Protocol 203.

<u>Term</u>	<u>Definition</u>
VIGOR	<u>Vioxx Gastrointestinal Outcomes Research.</u> Double-blind study by MRL assessing the comparative efficacy and gastrointestinal safety of Vioxx 50 mg and naproxen 1000 mg; found a statistically significant decrease in PUBs among patients on Vioxx and a statistically significant difference in cardiovascular adverse events favoring naproxen.
Vioxx Adverse Experience Review Team (AERT)	At Merck, three-person cross-functional team that met every six months to review spontaneously reported post-marketing adverse events among patients on Vioxx.
Vioxx Commercialization Team (Vioxx CST)	At Merck, a cross-functional committee that participated in developing the commercialization strategy for Vioxx.
Vioxx CST	<u>See “Vioxx Commercialization Team”</u>
ViP	<u>Effects of Rofecoxib in Reducing the Risk of Prostate Cancer.</u> Placebo-controlled study of the efficacy of Vioxx 25 mg in reducing the risk of prostate cancer; also called Protocol 201. One of three studies that comprised Protocol 203.
WAE	<u>See “Worldwide Adverse Experiences”</u>
WAES	<u>See “Worldwide Adverse Event System”</u>
WBST	<u>See “Worldwide Business Strategy Team”</u>
WCDMO	<u>See “Worldwide Clinical Data Management Operations”</u>
WCQAR	<u>See “Worldwide Clinical Quality Assurance Resources”</u>
Worldwide Adverse Experience System (WAES)	Merck database of all adverse events experienced by patients on Merck drugs that are spontaneously reported post-marketing or that arise in the course of a Merck-sponsored clinical trial.

<u>Term</u>	<u>Definition</u>
Worldwide Business Strategy Team (WBST)	Merck cross-functional committee charged with formulating development and marketing strategies for the Company's products.
Worldwide Clinical Data Management Operations (WCDMO)	Merck department that maintains the Clinical Trial System.
Worldwide Clinical Quality Assurance Resources (WCQAR)	Subdivision of MRL responsible for auditing Merck's clinical trials to ensure compliance with Merck's SOPs; department merged into Worldwide Product Safety and Epidemiology in early 2004.
Worldwide Human Health Marketing (WHHM)	Organization within Merck responsible for marketing Vioxx and other Merck products abroad.
Worldwide Marketing Application (WMA)	Standardized application accepted by many different regulatory authorities around the world for permission to market a drug for use on humans for treatment of a given disease state or symptoms.
Worldwide Product Circular Review Team (WPCRC)	Merck team that considered and proposed changes to product label.
Worldwide Product Safety and Epidemiology (WPS&E)	Subdivision of MRL responsible for analyzing and reporting post-marketing adverse events.
WPCRC	<u>See</u> "Worldwide Product Circular Review Team"
WPS&E	<u>See</u> "Worldwide Product Safety and Epidemiology"
WHHM	<u>See</u> "Worldwide Human Health Marketing"
Zocor	Merck drug (simvastatin) for the treatment of high cholesterol.

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