The present invention relates to the detection of markers in exhaled breath, wherein the detection of the presence or absence of the marker(s) in exhaled breath is used to assess various clinical data, including patient adherence in taking the medication and patient enzymatic (metabolic) competence in metabolizing the medication. An embodiment of the invention comprises a parent therapeutic agent labeled with a marker, whereupon metabolism (e.g., via enzymatic action) of the therapeutic agent, the marker becomes volatile or semi-volatile and is present in the breath. In certain related embodiments, the marker contain a deuterium label, which is also present in the breath upon metabolism of the therapeutic agent. In another embodiment of the invention, the therapeutic agent is associated with a taggant (that may be either labeled or unlabeled with deuterium), which in turn will generate a marker in the breath that is easily measurable.
Abstract

The present invention relates to the detection of markers in exhaled breath, wherein the detection of the presence or absence of the marker(s) in exhaled breath is used to assess various clinical data, including patient adherence in taking the medication and patient enzymatic (metabolic) competence in metabolizing the medication. An embodiment of the invention comprises a parent therapeutic agent labeled with a marker, where upon metabolism (e.g., via enzymatic action) of the therapeutic agent, the marker becomes volatile or semi-volatile and is present in the breath. In certain related embodiments, the marker contain a deuterium label, which is also present in the breath upon metabolism of the therapeutic agent. In another embodiment of the invention, the therapeutic agent is associated with a taggant (that may be either labeled or unlabeled with deuterium), which in turn will generate a marker in the breath that is easily measurable.
DEMANDES OU BREVETS VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 3

NOTE: Pour les tomes additionels, veillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE THAN ONE VOLUME.

THIS IS VOLUME 1 OF 3

NOTE: For additional volumes please contact the Canadian Patent Office.
DESCRIPTION

MEDICATION ADHERENCE MONITORING SYSTEM

FIELD OF INVENTION

The present invention relates to marker detection, in the form of odors or the like, to monitor medication adherence, and, more particularly, to a method and apparatus for the detection of markers in exhaled breath after the medication is taken by a patient, wherein such markers are combined with the medication.

BACKGROUND INFORMATION

Breath is a unique bodily fluid. Unlike blood, urine, feces, saliva, sweat and other bodily fluids, it is available on a breath to breath and therefore continuous basis. It is readily available for sampling non-invasively. Because the lung receives nearly 100% of the blood flow from the right side of the heart and has an anatomical structure (e.g., an alveolar-capillary membrane that is only 200-1000 nm thick and separates the blood from the gas in the lungs) that contains a massive surface area for effective diffusion of gases (e.g., transport oxygen and carbon dioxide), it has been suggested that the concentration of analytes/compounds in breath not only correlate with their blood concentrations, but will also rapidly change to sudden changes in analyte/compound concentrations in the blood. Other positive aspects of sampling the breath, as opposed to other bodily fluids, is that breath is less likely to be associated with the transfer of serious infections, is less intrusive to subjects who require the collection of biological samples (e.g., urine collection for drug testing), and is preferred by individuals who collect biological samples from subjects for health care assessments and/or drug testing (e.g., health care providers drawing blood or collecting urine, saliva and other non-breath biological media). Further, the collection of breath samples is relatively straightforward and painless.

The breath is comprised of two components: 1) a gas phase, and 2) a liquid phase. The liquid phase of breath is formed by aerosol droplets plus condensed water from the gas phase. Exhaled breath contains nearly 100% humidity at 37°C (body temperature). The aerosol droplets in exhaled breath are likely formed from the bulk flow of air over the airway lining fluid (ALF), which is a thin layer of liquid that lines a significant portion of the airway passages in the lung. The ALF can be considered an ultrafiltrate of blood, and allows
transport of molecules from one side of the alveolar-capillary membrane to the other, either by (1) transmembrane passage (e.g., most uncharged, lipophilic molecular entities) and/or by transport through paracellular spaces located between cells that doesn't require transport directly through cell membranes (e.g., most charged and/or highly water soluble molecular entities). Therefore, not surprisingly, a wide variety of analytes/compounds with different properties (e.g., volatile, semi-volatile, non-volatile, hydrophobic, hydrophilic, charged, uncharged, small and large) that are in the blood can rapidly cross the capillary-alveolar and appear in the breath. If the temperature of the collected sample is maintained at 37°C or higher, volatile or semi-volatile analytes, particularly those that are relatively insoluble in water and readily diffuse out of water, will preferentially remain in the gas state of breath and can be treated as a gas for compounds. In this instance, sensors designed to work with gaseous media would be preferable. For compounds that are highly water soluble and likely to remain in solution, the exhaled breath sample can be collected as a condensate when cooled. This liquid can then be analyzed with sensors that are designed for liquid-based analyses. Compounds likely to be detectable in the gas phase typically are lipophilic (hydrophobic) and semi-volatile or volatile molecules such as the intravenous anesthetic agent, propofol (vapor pressure ~ 0.2 mmHg at 37 °C), while compounds likely to be detected in the liquid phase are hydrophilic, non-volatile and/or significantly charged at physiological pH (normal pH =7.4), such as glucose, lactic acid, most therapeutic agents and electrolytes (e.g., Cl⁻, Na⁺, K⁺, Ca²⁺, Mg²⁺). Thus an exhaled breath sample can be handled to produce a gaseous matrix for certain compounds and sensors, and a liquid matrix for others. In instances where it is desirable to detect more than one compound (e.g., detection of hydrophilic and hydrophobic molecules in the breath), the sample can be split and a portion maintained as a gas and a portion condensed as a liquid.

Medication non-compliance (or non-adherence) is the failure to take drugs on time in the dosages prescribed, which results in patient undermedication or overmedication. Lack of medication adherence is as dangerous and costly as many illnesses. As any physician or caregiver understands, medicine is only effective when taken as directed.

Noncompliance cuts across all categories of patients and illnesses. People with breast cancer, organ transplants, and hypertension, as well as people on a short course of antibiotics, can all forget to take their medications. Researchers have identified more than 200 variables
that affect whether a patient will be compliant. Compliance rates are also likely to decline over time, especially for patients with asymptomatic diseases.

Non-compliance of patients to drug regimens prescribed by their physicians results in excessive healthcare costs estimated to be around $100 billion per year through lost workdays, increased cost of medical care, higher complication rates, as well as drug wastage. Studies have shown that non-compliance causes 125,000 deaths annually in the U.S. alone [Smith, D., “Compliance Packaging: A Patient Education Tool,” *American Pharmacy*, NS29(2) (1989)]. Moreover, medication non-adherence leads to 10 to 25 percent of hospital and nursing home admissions, and is becoming an international epidemic [Standberg, L.R., “Drugs as a Reason for Nursing Home Admissions,” *American Healthcare Association Journal*, 10(20) (1984); Schering Report IX, *The Forgetful Patient: The High Cost of Improper Patient Compliance; Oregon Department of Human Resources, A study of Long-Term Care in Oregon with Emphasis on the Elderly*, (March 1981)].

About 50% of the 2 billion prescriptions filled each year are not taken correctly [National Council for Patient Information and Education]. 1/3 of patients take all their medicine, 1/3 or patients take some dosage of the prescribed medicine, 1/3 of patients do not take any at all [Hayes, R.B., *NCPIE Prescription Month*, (October 1989)]. Such sub-optimal rates of compliance reported by various studies becomes of even greater concern as the American populace ages and becomes more dependent on drugs to fight the illnesses accompanying old age. By 2025, over 17% of the US population will be over 65 [Bell JA, May FE, Stewart RB: Clinical research in the elderly: Ethical and methodological considerations. *Drug Intelligence and Clinical Pharmacy*, 21: 1002-1007, 1987] and senior citizens take, on average, over three times as many drugs compared to the under 65 population [Cosgrove R: Understanding drug abuse in the elderly. *Midwife, Health Visitor & Community Nursing* 24(6):222-223, 1988]. The forgetfulness that sometimes accompanies old age also makes it even more urgent to devise cost-effective methods of monitoring compliance on a large scale.

Further, non-compliance of patients with communicable diseases costs the public health authorities millions of dollars annually and increases the likelihood of drug-resistance, with the potential for widespread dissemination of drug-resistant pathogens resulting in epidemics. For example, one of the most serious consequences of noncompliance involves the outbreaks of new, drug-resistant strains of HIV and tuberculosis (TB), which have been
significantly attributed to patients who do not properly follow their complex medication regimens. In addition, the long-term misuse of antibiotics has given rise to forms of previously treatable diseases that are impervious to the most advanced medications.

Current methods of improving medication adherence for health problems are mostly complex, labor-intensive, and not predictably effective [McDonald, HP et al., “Interventions to enhance patient adherence to medication prescriptions: scientific review,” JAMA, 289(4):3242 (2003)]. A cost-effective, but difficult to administer, program has been developed in seven locations around the nation to combat this serious threat to the American populace. It involves direct observation of all drug delivery by trained professionals (directly observed therapy; DOT) but is impractical for large scale implementation. Many techniques are also invasive, e.g., blood sampling.

Previous medication adherence monitoring systems disclosed by the present inventors related to the use of exhaled breath as a means to detect when and/or whether a subject has taken medication as prescribed (see, for example, U.S. Patent Application Serial Nos. 7,820,108 issued November 26, 2010 and US 2005-0233459 A1 published October 20, 2005. The monitoring systems described in those applications either detected in exhaled breath the medication; a metabolite of the medication; or a detectable marker (that was combined with the medication) or its metabolite. Many of the markers considered for use in those applications were largely GRAS (“Generally Recognized As Safe”) compounds, as classified by the FDA. Unfortunately, currently available detectors (sensors) do not detect these compounds in exhaled breath reliably (e.g., issues due to sensitivity or discrimination from potential interferents) to be used in practical devices for many medication adherence applications.

Accordingly, there is a need in the art for a system and method to improve drug compliance which provides simple monitoring of medication dosing which is non-invasive, intuitive and sanitary. In particular, there is a need for a unique group of markers that can be combined with medications for adherence monitoring, where the markers are sufficiently volatile to be detected in the gas phase of exhaled breath, even at very low concentrations using current detection technologies.
SUMMARY OF THE INVENTION

The present invention solves the needs in the art by providing systems and methods for non-invasive monitoring of medication adherence by detecting a marker in exhaled breath that is the product of medication absorption, distribution, metabolism, and/or excretion in the patient’s body.

BRIEF DESCRIPTION OF THE FIGURES

For a more complete understanding of the present invention, and the advantages thereof, reference is now made to the following descriptions taken in conjunction with the accompanying drawings, in which:

Figures 1-59 illustrate various aspects of the invention relating to the use of isotopic labels as detectable markers for monitoring patient medication adherence.

Figure 1 shows hydrolysis reactions of the esterase type - carboxylic ester hydrolases (EC 3.1.1).

Figure 2 show illustrative examples of select alcohols and their physiochemical properties.

Figure 3 show illustrative examples of carboxylic acids and their physiochemical properties.

Figure 4 show dealkylation reactions by CYP450 (Example: Demethylation).

Figure 5 show physicochemical and toxological properties of select aldehydes.

Figure 6A shows metabolic fate of selected ordinary isotope-labeled alcohols, aldehydes, and carboxylic acids.

Figure 6B shows a non-ordinary isotope-labeled alcohols, aldehydes and carboxylic acids.

Figure 7A shows illustrative examples of therapeutic agents undergoing desmethylation and generating formaldehyde.

Figure 7B shows illustrative examples of therapeutic agents undergoing desmethylation and generating formaldehyde.

Figure 8 shows illustrative examples of therapeutic agents undergoing desethylation and generating acetaldehyde.

Figure 9 shows illustrative examples of therapeutic agents undergoing despropylation and generating propionaldehyde.
Figure 10A-B show illustrative examples of therapeutic agents undergoing desbutylation and generating butyraldehyde, including an illustration of butyraldehyde.

Figure 11 shows a gas phase FTIR-based absorption spectrum of human breath.

Figure 12 shows a gas phase FTIR-based absorption spectrum of ethanol in nitrogen gas.

Figure 13 shows a gas phase FTIR-based absorption spectrum of d5 ethanol in nitrogen gas.

Figure 14 shows a gas phase FTIR-based absorption spectrum of d2 ethanol in nitrogen gas.

Figure 15 shows a gas phase FTIR-based absorption spectrum of ethanol, d5 ethanol, and d2 ethanol in nitrogen gas.

Figure 16 shows a gas phase FTIR-based absorption spectrum of methanol, ethanol, d3 methanol, and d5 ethanol in nitrogen gas.

Figure 17 shows a gas phase FTIR-based absorption spectrum of d2 ethanol in human breath.

Figure 18 shows a gas phase FTIR-based absorption spectrum of d2 ethanol in human breath with background breath absorption subtracted.

Figure 19 shows a gas phase FTIR-based absorption spectrum of acetaldehyde and d4 acetaldehyde in nitrogen gas.

Figure 20 shows a gas phase FTIR-based absorption spectrum of d5 ethanol and d4 acetaldehyde in nitrogen gas.

Figure 21 shows a gas phase FTIR-based absorption spectrum of d5 ethanol and d4 acetaldehyde in human breath.

Figure 22 shows a gas phase FTIR-based absorption spectrum of benzene (C₆H₆), ¹³C-labeled benzene (¹³C₆H₆), and deuterated benzene (C₆D₆) in nitrogen gas.

Figure 23 shows a gas phase FTIR-based absorption spectrum of acetaldehyde and ¹³C-labeled acetaldehyde (¹³CH₃¹³CHO) in nitrogen gas.

Figure 24 shows a gas phase FTIR-based absorption spectrum of formaldehyde and d2 formaldehyde in nitrogen gas.

Figure 25 shows a gas phase FTIR-based absorption spectrum of acetaldehyde and d4 acetaldehyde in nitrogen gas.
Figure 26 shows a proposed FTIR deuterium labeled spectral monitoring bands to distinguish deuterated ethanol, deuterated acetaldehyde, and deuterated benzene in nitrogen gas.

Figure 27 shows proposed FTIR deuterium labeled spectral monitoring bands to distinguish d3 methanol, d5 ethanol, d4 acetaldehyde, d6 benzene, and d8 styrene in Nitrogen gas.

Figure 28 shows illustrative examples of amines that appear in food.

Figure 29 shows an ester example of a GRAS agent listed as food additive (Class 1 Drug) – Aspartame: An ester food additive metabolized by human gut esterases and gut peptidases.

Figure 30 shows an esterase example of a FDA Approved Drug (Class 2 Drug) - Aspirin (Acetylsalicylic Acid): An ester drug metabolized by aspirin esterases in humans.

Figure 31 shows an ester example of GRAS agents listed As food additives (Class 1 Drugs) – methyl, ethyl, propyl and butyl parabens: ester food additives metabolized by human carboxylesterases and tissue esterases.

Figure 32 shows an esterase example of a FDA approved drug (Class 2 Drug) - Clofibrate: An ester drug metabolized by esterases in humans.

Figure 33 shows an esterase example of a FDA approved drug (Class 2 Drug) – Esmolol: A drug metabolized by arylolesterase located within the cytosol of human red blood cells.

Figure 34 shows an example of an ester FDA Approved Drug (Class 2 Drug) – Procaine: An ester drug metabolized by pseudocholinesterase (butyrylcholinesterase) located within human blood.

Figure 35 shows an example of an esterase creation of new chemical entity (NCE) (Class 3 Drug) – Cyclic Structure Containing Three Ester Groups.

Figure 36 shows an example of an esterase creation of new chemical entity (NCE) (Class 3 Drug) – Linear structure containing three ester groups.

Figure 37 shows an example of an esterase creation of new chemical entity (NCE) (Class 3 Drug) – Linear structure containing four ester groups.

Figure 38 CYP450 Example 1 – CYP-3A4-mediated Metabolism FDA Approved Drug (Class 2 Drug): Verapamil – An L-type Calcium Channel Blocker.
Figure 39 shows CYP450 Example 2 – CYP-3A4-mediated Metabolism FDA Approved Drug (Class 2 Drug): Erythromycin – An Antibiotic.

Figure 40 shows CYP450 Example 3 – CYP-3A4-mediated Metabolism FDA Approved Drug (Class 2 Drug): Amiodarone – An Antiarrhythmic Drug.

Figure 41 shows CYP450 Example 4 – CYP-3A4-mediated Metabolism FDA Approved Drug (Class 2 Drug): Propafenone – An Antiarrhythmic Drug.

Figure 42 CYP450 Example 5 - CYP-3A4-mediated Metabolism FDA Approved Drug (Class 2 Drug): Diltiazem – An Antiarrhythmic Drug.

Figure 43 CYP450 Example 6 - CYP-2D6-mediated Metabolism FDA Approved Drug (Class 2 Drug): Flecainide – An Antiarrhythmic Drug.

Figure 44 shows CYP450 Example 7 - CYP-2D6-mediated Metabolism FDA Approved Drug (Class 2 Drug): Codeine – A Prodrug Narcotic for Analgesia.

Figure 45 shows CYP450 Example 8 - CYP-1A2-mediated Metabolism FDA Approved Drug (Class 2 Drug): Olanzapine – An Antipsychotic Agent.

Figure 46 shows CYP450 Example 9 - CYP-1A2-mediated Metabolism Class 1 Drug: Caffeine – A Food Additive.

Figure 47 shows CYP450 Example 10 - CYP-2C-mediated Deamination FDA Approved Drug (Class 2 Drug): Amphetamine – A CNS Stimulant.

Figure 48 shows Deamination Example 1 – Adenosine Deaminase (EC 3.5.4.4) mediated Deamination FDA Approved Drug (Class 2 Drug): Adenosine – An Antiarrhythmic Agent.

Figure 49A-C shows MAMS: Illustrative Examples – Simple Approaches.

Figure 50A-B shows MAMS: Illustrative Examples – Approaches of Intermediate Complexity.

Figure 51A-B shows MAMS: Illustrative Examples – Approaches of Intermediate Complexity.

Figure 52 shows MAMS: Illustrative Examples – Complex Approaches.

Figure 53 shows MAMS: Illustrative Examples – Complex Approaches.

Figure 54 shows MAMS: Illustrative Examples – Complex Approaches.

Figure 55 shows MAMS: Illustrative Examples – Complex Approaches.

Figure 56A-D shows a hypothetical example – an illustration of how MAMS-11 would function.
Figure 57A-C shows MAMS: illustrative examples – one drug with many doses, Type 1.

Figure 58A-C shows MAMS: illustrative examples – one drug – many doses, Type 2.

Figure 59A-C shows MAMS: illustrative examples – one drug – many doses, Type 3.

**DETAILED DESCRIPTION**

The means to practice medication adherence monitoring in accordance with the subject invention are based on the development and use of markers as categorized below:

**Class 1:** Generally recognized as safe (GRAS) compounds including but not limited to food additives/components in industrialized countries and agents listed on the FDA inactive ingredient database;

**Class 2:** Drugs already approved by governmental regulatory authorities (e.g., FDA) as therapeutic agents;

**Class 3:** New chemical entities (NCEs) including those from slightly modified derivatives of Class 2 agents (e.g., chemically modified verapamil or dextromethorphan) or those derived from completely new chemical scaffolds (e.g., fluoroesters).

There are a variety of strategies for using Class 1, 2 and 3 marker compounds to assess whether a subject took his/her medication as prescribed by their health care provider. Central to all of these approaches is generation of a volatile (including semi-volatile or poorly volatile) chemical marker that appears in body fluids, preferably in the breath, hereafter termed the exhaled drug ingestion marker (EDIM). EDIMs arise from a number of sources or combination of sources, including:

**EDIM Source 1:** any component of the active therapeutic drug matrix. The active therapeutic drug matrix contains three different components: 1) the active drug itself (Source
1) any associated salts (Source 1S) linked to the active drug (e.g., mesylate, acetate, tartrate, succinate, etc.), and 3) excipients (Source 1E).

**EDIM Source 2:** metabolite(s) of the active therapeutic drug matrix, including active drug (Source 2A), salt (Source 2S), and/or excipients (Source 2E).

**EDIM Source 3:** a compound that is associated with the active therapeutic drug matrix but is not an integral part of it per se, hereafter termed a taggant (i.e., the taggant is physically located adjacent but not physically integrated into the active therapeutic drug matrix).

**EDIM Source 4:** a metabolite of the taggant.

Thus, according to the subject application, an EDIM could be liberated from as many as 8 general sources within a therapeutic (such as a pill) system. However, the exact number of EDIM sources in a given therapeutic system will be dependent upon other factors, including whether more than one excipient of the active therapeutic drug matrix is used as an EDIM source (usually more than one excipient is added to the final formulation) and/or whether more than one taggant is added to the pill system as EDIM sources, either from themselves or their metabolites. Similarly, since a number of therapeutic pills contain more than one active therapeutic agent (combination therapy) such as the anti-cholesterol agent Vytorin (ezetimibe and simvastatin), additional EDIM sources may arise from them or their metabolites.

For example, if the EDIM is a metabolite, it is most likely generated by enzymatic degradation but could also occur by spontaneous breakdown of compounds in the human body independent of specific enzyme action. The enzyme metabolism of many Class 1 through 3 agents to volatile (including semi-volatile or poorly volatile) EDIMs in the breath is well known, predictable or easily tested in various *in vitro* and *in vivo* systems. Humans contain a great variety of enzymes (Table 1) that can generate potential EDIMs. Examples include esterase-mediated degradation of esters (e.g., fluoroesters → fluoroalcohols + carboxylic acids) to their corresponding alcohols and carboxylic acids, alcohol dehydrogenase mediated degradation of 1° and 2° alcohols to their respective aldehydes and ketones, respectively; or CYP-mediated reactions via reduction, oxidation and/or hydrolysis to generate volatile (including semi-volatile or poorly volatile) metabolites (e.g., aldehydes via CYP-mediated dealkylation reactions). These will be discussed in greater detail below with specific examples illustrated. As shown above, different combinations of compounds
(drug class 1, 2 and/or 3), which are enzymatically degraded by a wide variety of enzymes (e.g., esterases, dehydrogenases, CYP-450 fractions, deaminases), can be incorporated into a pill system that can potentially generates 8 different general EDIM sources (1A, 1S, 1E, 2A, 2S, 2E, 3, and 4). This architecture of the pill system allows the construction of several types of highly flexible, adaptable medication adherence monitoring system (MAMS) configurations.

The EDIM is a molecular entity that could either be naturally found in the body (endogenous) but be detected at concentrations that readily distinguish it from natural background breath levels for the MAMS application, or is unique (not endogenous to the human body) and can very easily distinguished in human breath. With regard to the latter, the incorporation of an isotope(s) into the EDIM or the compound (Class 1, 2 and/or 3 agent) that generates the EDIM, particularly those that are stable (non-radioactive) and not ordinary (i.e., not the most abundant form of atom found in nature) to a specific atom (e.g., deuterium at the hydrogen atom) to MAMS chemistry offers a multitude of major advantages. These include excellent chemistry flexibility (multiple isotopic labeling targets on various molecules), outstanding signal-to-noise ratio (labeled EDIMs would be easily distinguished against endogenous compounds that are not labeled with non-ordinary isotopes such as deuterium, which likely removes the need for baseline breath sampling), excellent safety in humans (selective isotopic labeling does not significantly alter the physiochemical/molecular properties of the molecule), and minimal-to-no effects on pharmacokinetics (absorption, distribution, metabolism, elimination [ADME]/pharmacokinetics [PK]) or pharmacodynamics (PD) of the active drug. These characteristics of an isotope-based MAMS indicate it would be able to navigate the regulatory “waters” (pathways) much more easily, be less complex, and be less expensive but yet be more reliable in its use and have a shorter time to market.

With regard to isotope-labeled EDIMs, the need for a baseline sample is predicated on the incidence of the non-ordinary isotope in nature (Table 2). Since the incidence of deuterium (\(^\text{2}^\text{H}\)) among H isotopes (0.015%) and \(^{17}\text{O}\) among O isotopes (0.037%) in nature is very low, the baseline sampling requirement here would be minimal compared to that of \(^{13}\text{C}\) among C isotopes (1.11%). In other words, the chances of isotopic background noise (non-ordinary isotopes that appear normally in nature and in the body) interfering with an isotopic-labeled EDIM measurement is 74-fold (=1.11%/0.015%) or 30-fold (=1.11%/0.037%) greater for a \(^{13}\text{C}\)-based label than for a deuterium-based or \(^{17}\text{O}\)-based EDIM labels, respectively. For
these reasons, a preferred isotopic label for the current invention is deuterium. The EDIM-based isotopic (non-ordinary isotope) labels suitable for biological applications include but are not limited to those shown in Table 2. Similar to the case of non-isotopic (or known as ordinary isotopes) labeled EDIMs, isotopic labeled EDIMs may or may not require the action of enzymes (Table 1). Hereafter, the term labeled (e.g., labeled compound or labeled EDIM) or isotope in this application denotes the use of a “non-ordinary” isotope of an atom.

Current methods for adapting isotopes (both non-radioactive and radioactive) in clinical medicine can be applied to the subject invention. For example, breath tests using $^{13}$C, $^{14}$C to assess enzyme function, using $^{15}$N to improve the quality of biochemical tracer studies, or using $^{17}$O (for MRI scans) or $^{18}$O (for PET scans) to improve the quality of imaging can be applied to the subject invention.

For example, breath tests that require the oral or intravenous administration of $^{13}$C-labeled caffeine (Park-GJH et al, Hepatology 38:1227-1236, 2003) and intravenous administration of $^{14}$C-labeled erythromycin (US Patent 5,100,779) can be used to assess medication adherence by measuring the amount of carbon isotope-labeled carbon dioxide in the breath produced at various times or a fixed time post administration of a labeled drug/therapeutic of the invention. Table 2 depicts a variety of biologically relevant isotopes that could be useful for MAMS. By illustrating how various isotopic labels, preferably those that are stable (non-radioactive) including deuterium ($^2$H), can be incorporated into the EDIM (EDIM Sources 1 [1A, 1S, 1E], 2 [2A, 2S, 2E], 3, and 4) and adding new embodiments, the current application will further teach and expand on the principle of applying isotopic labeling to medication adherence monitoring systems (MAMS).

Overview of MAMS using isotopes

According to the subject application, isotope-based MAMS preferably contain 3 elements:

**Element 1 - medical chemistry:** targeted, stable isotopic labeling, ideally with non-radioactive isotopes shown in Table 1 (most preferably with deuterium) of Class 1, 2 and/or 3 compounds that provide EDIM(s) from EDIM Sources 1 (1A, 1S, 1E), 2 (2A, 2S, 2E), 3, and/or 4. In another embodiment, to maximize the number of different active therapeutic drugs that could be identified with MAMS, combinations of isotopic (e.g., deuterium)-labeled EDIMs could be combined in various ways with non-isotopic (e.g., ordinary hydrogen) EDIMs. The
reviewer is referred below to the discussion in Element 2 for additional details on how isotopic chemistry will be used for MAMS.

**Element 2 - sensor:** a variety of sensors modalities to measure the EDIM in breath were previously discussed in the prior patent applications listed in Introduction (Section A). According to the subject invention, preferred sensor embodiments include those that have the ability to measure isotopic-based EDIMs, such as gas chromatography detectors coupled to infrared-based detectors or gas chromatography mass spectroscopy sensors. More preferably, the sensor embodiments can comprise modified and optimized commercial off-the-shelf (COTS) miniature gas chromatography (mGC) detector coupled to infrared (IR, liquid based for detection of poorly volatile isotopic-labeled EDIMs and/or gas based for detection of volatile or semi-volatile EDIMs) detection capabilities. This sensor will allow chromatographic separation of various EDIMs while simultaneously exploiting the powerful infrared (IR) spectroscopy (difference in mass among molecules containing isotopes have different vibrational modes) analytical capabilities to distinguish endogenous analytes from isotopic (preferably deuterated) ones. Alternately, a portable GC-MS would be suitable. Portable GC-MS could distinguish various isotopic labels (since isotopes have different masses) and thus greatly increase the number of taggants.

In contrast, IR alone would unlikely be able to discriminate between deuterated compounds of a given chemical class such as aliphatic alcohols (e.g., methanol versus ethanol) or aldehydes (e.g., formaldehyde versus acetaldehyde). The study of alcohols is important because a number of chemical classes, including but not limited to esters, carbonate esters, acetals, or ketals may be the optimal sources (e.g., chemistry flexibility, safety, etc.) for generating EDIMs with ideal characteristics for MAMS applications. As shown in Figure 1, an ester is hydrolyzed to its corresponding alcohol and carboxylic acid. Other chemical classes that can also enzymatically or spontaneously create alcohols include carbonate esters, acetals and ketals. Esters, carbonate esters, acetals and ketals can belong to Class 1, 2 or 3 (see Section A for classification).

In the embodiment illustrated in Figure 1, depending upon the ester, the EDIM(s) could be 1) an isotopic-labeled ester, 2) an isotopic-labeled alcohol derived from the isotopic-labeled ester, 3) an isotopic-labeled acid derived from the isotopic-labeled ester, and 4) an isotopic-labeled aldehyde or ketone derived from an isotopic-labeled 1° or 2° alcohol, which may or may not be generated from 1° or 2° alcohol-based esters, respectively. In addition,
various combinations of isotopic-labeled esters and their associated labeled acids, labeled alcohols and/or labeled aldehydes/ketones could be used to provide unique EDIM signatures in the breath. The type of R2 group in the ester can be varied to sterically/electronically alter the susceptibility of the ester to hydrolysis, and will thus play a significant role in the rate of appearance of ester-derived labeled EDIM(s). The physicochemical properties (e.g., physical state, volatility) of the ester will be a function of both R1 and R2. By incorporating various isotopic labels listed in Table 2 (preferred embodiment is deuterium), where appropriate, into the various atomic sites of the esters, various EDIMs (arising from the ester, acid, alcohol and/or aldehyde/ketone) containing one or more isotopic labels could be generated that will fulfill the requirements of an effective MAMS.

As shown in Table 2, a number of isotopes can be placed on key parts of ester molecules to liberate products (alcohols and/or acids) via ester hydrolysis that contain distinctive isotopic tags. The structures and key physicochemical characteristics of relevant alcohols and acids that may serve as isotopic-labeled EDIMs for MAMS are shown in tables in Figures 2 and 3, respectively. Figure 2 illustrates examples of select alcohols and their physicochemical properties. Figure 3 shows different carboxylic acids that are commonly generated via enzymatic degradation of GRAS-type flavoring additives and/or FDA approved drugs (e.g., esterase mediated degradation of esters to their corresponding acids and alcohols). Furthermore, as stated previously, the 1° and 2° alcohols will in turn be further metabolized by alcohol dehydrogenase to yield aldehydes and ketones, respectively. In an identical manner to that described above for esters, similar compounds, including but not limited to carbonate esters, acetals, and ketals could be labeled to generate alcohols (and subsequent generation of aldehydes/ketones) and/or carboxylic acids.

The study of aldehydes is important because the CYP450 enzyme system, which is by far the most important enzyme system for degrading drugs in humans predominantly via the processes of reduction, oxidation and hydrolysis, frequently generate different aldehydes via various types of dealkylation reactions. Among the different types of dealkylation reactions (Figure 4), demethylation (desmethyl metabolites via O-, N- and S-demethylation), which produces formaldehyde, is most notable. However, other important dealkylation reactions in human drug metabolism include deethylation (desethyl metabolites), depropylation (despropyl metabolites) and debutylation (desbutyl metabolites) reactions that generate...
acetaldehyde, propionaldehyde and butyraldehyde, respectively. The CYP450 substrates can belong to Class 1, 2 or 3 (see Section A for classification).

The structures and key physicochemical characteristics of some relevant aldehydes that may serve as isotopic-labeled EDIMs for MAMS are shown in Figure 5. Further metabolism of the primary alcohols, acids, and aldehydes discussed above is via the tricarboxylic acid (TCA) cycle, which will ultimately produce carbon dioxide and water as illustrated in the reaction scheme of Figure 6. On the other hand, shorter branched-chain aliphatic alcohols, aldehydes, and acids undergo beta-oxidative cleavage to yield intermediates of the amino acid and/or fatty acid metabolic pathways, which undergo subsequent complete metabolism to CO₂ and water via the tricarboxylic acid cycle. As chain length and substitution increase, the alcohols and aldehydes undergo a combination of omega-, omega-1 and beta-oxidation, and selective dehydrogenation and hydration to yield polar acidic metabolites. Numerous specific illustrative examples of how Class 1, 2 and/or 3 agents, which are degraded by different enzyme systems, can be used as isotope-labeled EDIMs per se or to liberate isotopic-labeled EDIMs for an effective MAMS will be shown in Section C. Examples of FDA-approved drugs that generate formaldehyde (Figure 7), acetaldehyde (Figure 8), propionaldehyde (Figure 9) and butyraldehyde (Figure 10) via CYP450-mediated demethylation, desethylation, despropylation, and desbutylation, respectively, are illustrated.

The isotopic labeling of molecular entities that serve as isotope-labeled EDIMs themselves, or of substrates that, via enzymatic degradation, liberate isotopic-labeled EDIMs, is a critically important strategy toward designing and developing an optimal MAMS. In a series of experiments (Figures 11-27) using a gas phase Fourier Transform Infrared (FTIR) device (Nicolet 6700 FT-IR, 5 liter Breath Sample, 22 meter path length) using human breath and a nitrogen environment, key scientific assumptions that underlie the advantages listed above were tested for isotopic labeling in MAMS. Specifically investigated was the effect of non-ordinary isotopic (e.g., deuterium, ¹³C; see Table 2) labeling on the FTIR spectrum of key alcohols and aldehydes on the FTIR spectrum, relative to those containing ordinary isotopes at room temperature. Important findings include: 1) FTIR poorly discriminates between deuterated and ordinary alcohols of similar structure; the FTIR absorption spectrum for ordinary methanol and ethanol as well as deuterated methanol and ethanol are very similar. 2) FTIR spectra for a given alcohol (ordinary vs deuterated) is highly distinctive and
can be used to discriminate among them (i.e., CD$_3$-OH vs CH$_3$-OH or CD$_3$D$_2$-OH vs CH$_2$CH$_2$-OH). In contrast, GC-MS can easily distinguish between all these species. A gas chromatograph, including a miniature gas chromatograph (mGC), can easily distinguish between specific alcohols but not among deuterated and non-deuterated alcohols of a given type.

3) FTIR does not provide a high degree of discrimination between deuterated and ordinary aldehydes of similar structure; the FTIR absorption spectrum for ordinary formaldehyde and acetaldehyde as well as deuterated formaldehyde and acetaldehyde are similar. 4) FTIR spectra for a given aldehyde (ordinary vs deuterated) is highly distinctive and can be used to discriminate among them (e.g., CD$_3$CDO vs CH$_3$CHO or CD$_2$O vs CH$_2$O).

Taken together, the results indicate that isotopic labeling shows great promise in the specific, selective and sensitive detection of EDIMs in human breath for MAMS. Liquid based IR measurements of many of the same analytes discussed in Figure 11-27 displayed a similar pattern of IR spectral shifts as that determined in the gas phase, indicating measurements of these and other analytes (e.g., larger isotopic-labeled metabolic fragments of Class 1, 2 and/or 3 drugs), which may not be volatile, may be feasible with liquid-based IR measurements using exhaled breath condensate (EBC). Note: In addition, we recently carried out identical FTIR using the ketone, acetone. We found that per deuterated acetone gave a highly distinctive spectra relative to ordinary acetone (data not shown). This shows that strategies to generate ketones from $^2$° alcohols and/or from $^2$° alcohol-based esters (e.g., isopropyl-based, 2-butyl-based, 2-pentyl-based esters) show great promise as EDIM, particularly because in humans they tend to persist in the blood and breath for longer periods of time, relative to aldehydes (see below for discussion).

In summary from the above gas phase FTIR experiments ((Figures 11-27)), it appears that at least 3 fundamentally different deuterated EDIMs could be distinguished by designing a tunable midIR laser (to measure C-D vibrational stretch) with a center wavenumber of approximately 2150 ± 10% range (wavenumber range: preferably 2000 to 2300 cm$^{-1}$). These EDIMs include: 1) carbonyl (e.g., acetone with per deuterations on methyl groups) – wave number preferably 2040 cm$^{-1}$; 2) aliphatic (e.g., 2-butanone with deuterations on non-alpha carbons – wavenumber preferably 2240 cm$^{-1}$), and 3) aromatic (e.g., benzaldehyde, with per deuterations on ring – wavenumber preferably 2290 cm$^{-1}$). By combining molecules with molecular attributes including carbonyl, aliphatic and/or aromatic properties, at least 6 different types of molecules could be readily detected using tunable or non-tunable mIR.
approaches: 1) carbonyl only, 2) aliphatic only, 3) aromatic only, 4) carbonyl + aliphatic, 5) carbonyl + aromatic; 6) aliphatic + aromatic, and 7) carbonyl + aliphatic + aromatic. With the use of other types of optical detection systems, including but not limited to quantum cascade lasers, lead salt lasers, frequency-combed based systems, cavity-enhanced optical frequency comb spectroscopy, mode-locked femtosecond fiber lasers, and virtually imaged phase array (VIPA) detectors, a very large numbers of analytes, particularly in the breath, could be potentially detected.

Element 3 - communication link and storage: HIPAA compliant information flow from the sensor to a monitoring entity to verify medication adherence and log data. This element was previously discussed in the prior patent applications listed in Introduction (Section A).

Characteristics of an isotope-based MAMS

The preferred embodiment of an isotope-based MAMS will be designed to function under the following constraints: 1) work with all oral dosing schedules, 2) function with all orally administered drugs, 3) use a sensor having the ability to detect and measure labeled-EDIM(s) in breath samples; preferably, the sensor is a modified and optimized device such as GC or mGC with IR capabilities, IR alone, or GC-MS, and 4) be potentially coupled to existing biometric technologies (including but not limited to fingerprint, facial geometry, retinal scan, facial blood flow, or video phone) if a high degree of certainty is required. Although in the preferred embodiment, MAMS would be developed for orally ingested drugs, it could be readily applied to other modes of drug delivery (e.g., intravenous, ophthalmologic). Also, in certain preferred embodiments, the sensor is portable and provides rapid sensitive and specific measurements of labeled (preferred isotope being deuterium)-EDIM(s) breath concentrations,

Chemistry of isotope-based MAMS

A complete isotopic-based MAMS using human breath requires that breath arising from the lungs interfaces with a sensor that measures a volatile (including semi-volatile or poorly volatile) marker, the isotope (Table 2)-labeled EDIM which is generated via different types of enzyme(s) (Table 1) following oral ingestion of a therapeutic agent and confirms
adherence. The isotopically-labeled EDIM could arise from isotopic labeling of either Class 1, 2 or 3 type drugs (Section A), or any combination of them. In order to generate an isotope-labeled EDIM, the isotope could be placed on Class I, 2 or 3 drugs in the following ways: 1) a single isotopic label on a single functional group in the molecule (e.g., including but not limited to a single deuteration to replace an ordinary H atom in a methyl group), 2) multiple isotopic labels on a single functional group in the molecule (e.g., multiple deuterations to replace all of the ordinary H atoms in a methyl group), and/or 3) combinations of 1 and 2 on greater than one functional group of the molecule.

A methyl group could be used as the functional group for isotope labeling; although, any chemical group including but not limited to ethyl, propyl, and/or butyl groups on Class 1, 2, and/or 3 molecules could be used as a functional group for isotope labeling. One of the preferred embodiments would be isotopic-labeled Class 1 (GRAS type) compounds including those approved as food additives in the United States (Table 3), inactive ingredient list (Table 4), and/or excipients (Table 5). In particular, food additives used in industrialized countries, including but not limited to the compounds listed in the following tables for esters (Table 6), aliphatic higher alcohols (Table 7), aromatic alcohols (Table 8), thioalcohols (Table 9), thiols (Table 9), fatty acids (Table 10), aliphatic higher aldehydes (Table 11), aromatic aldehydes (Table 12), ethers (Table 13), thioethers (Table 14), phenol ethers (Table 15), ketones (Table 16), phenols (Table 17), lactones (Table 18), terpenes (Table 19), aliphatic higher hydrocarbons (Table 20), furfurals (Table 21), indoles (Table 21), and isothiocyanate (Table 21). In addition, a number of other suitable compounds exist, including carbonate esters, acetalis and ketals. Examples of these chemical classes that are food components in industrialized countries are listed in the Leffingwell & Associates (Canton, GA) "Flavor-Base 2007."

Figure 28 lists twelve amines that are listed by the FDA as chemicals found in food. A number of drugs are amines, including antihistamines (e.g., chlorpheniramine), antipsychotics (e.g., chlorpromazine), decongestants (e.g., ephedrine and phenylephrine) and central nervous stimulants (e.g., amphetamines, methamphetamine, and methcathinone). Likewise, the active therapeutic drugs contained within many FDA approved medications (Table 22) have the potential themselves to liberate suitable EDIMs for MAMS. Examples of how isotope-labeled Class 2 and 3 molecules can serve as EDIMs will be illustrated in detailed below in Section C. Last, a number of preservatives (Table 23) are added to food stuffs to maintain
food quality and/or as excipients to lengthen drug life. The sources for the above compounds that are found in food, include the archives of regulatory agencies within industrialized countries such as the United States, European Union and Japan.

Not all the compounds listed in the tables would be proposed to be used for MAMS applications. Their use will be strictly governed by government regulations, toxicological information and performance characteristics with regard to MAMS function. In fact, a number of compounds, independent of taste or flavor, appear in food because they provide specific roles in food processing and/or are present as by-products in the manufacturing process of creating foods. The major functions of food additives include: acidity regulator, anticaking agent, antifoaming agent, antioxidant, bulking agent, carbonating agents, clarifying agents, colloidal agents, color, color retention agent, concentrate, emulsifier, firming agent, flavor enhancer, flour treatment agent, foaming agent, freezant, gelling agent, glazing agent, humectant, liquid freezant, packing gas, preservative, propellant, raising agent, stabilizer, sweetener, and thickener.

Development of Isotopic-Labeled EDIMs for MAMS

As described above and to summarize, the isotopic-labeled EDIM(s) can be generated by 8 different sources: the active therapeutic drug A, which is metabolized to a key metabolite A1 plus other irrelevant metabolites; a salt S, which is potentially metabolized to a key metabolite S1 plus other irrelevant metabolites; and drug excipient(s) E, which is potentially metabolized to a key metabolite E1 plus other irrelevant metabolites; and a taggant(s) without pharmacological activity called T, which is located outside the matrix of the active therapeutic agent (and thus does not alter the formulation of the active therapeutic drug that was approved by the FDA) is metabolized to a key metabolite T1 plus other irrelevant metabolites. These reactions are summarized below:

**Active Therapeutic Drug Matrix:**

- Active Drug: \( A \rightarrow A1 + \text{others} \)
- Drug salt: \( S \rightarrow S1 + \text{others} \)
- Drug Excipient: \( E \rightarrow E1 + \text{others} \)

**Taggant Compartment:**

- Taggant: \( T \rightarrow T1 + \text{others} \)

Option 1: EDIM Source \( I_A \) - Detection of A: MAMS would be designed to detect a single pharmaceutical, A. Specifically, an isotope-based MAMS using labeled A as the EDIM
would be used. In certain instances, A may be present in breath too long (many hours to
days) for adherence purposes, particularly with the emphasis of developing QD (oral dose
once per day) or BID (oral dose twice per day) drugs, and therefore, not discriminate when
individual doses were taken (due to long metabolic long half and minimal increase in plasma
concentrations with dosing), which is likely given that most drugs now used are given once or
twice daily.

Option 2: EDIM Source 2_A - Detection of A1: Option 2 (detection of an isotopic-
labeled EDIM as a major metabolite of A) has multiple advantages. First, if A1 were
promptly detected in breath, and were created by the action of a specific enzyme (e.g.,
enzyme located in the liver), it would guarantee drug ingestion since A would be absorbed
into the blood and sent to the liver for metabolism. In contrast, if the subject just “chewed”
the tablet in his/her mouth and tried to fool the system, the EDIM would not appear because
the enzyme is not located in the saliva. Second, this type of isotope-labeled EDIM, when
accurately quantitated with a breath sensor, would not only indicate medication adherence but
also create a “smart” (self monitoring and reporting therapeutic) drug that could potentially
report its own metabolism, and thus minimize the impact of adverse drug reactions (ADRs),
secondary to drug-drug interactions (DDIs), genetic abnormalities (polymorphisms) and/or
pathophysiological disturbances, in patients. Physiological factors that markedly increase or
decrease the isotope-labeled EDIM concentration in breath would indicate that the
metabolism of the active therapeutic agent (A) is being significantly altered and should be
promptly investigated, particularly if the EDIM breath concentration was stable for a
prolonged period of time before the change.

In one embodiment, the concentration of the Source 2_A EDIM could be used alone to
follow the in vivo metabolism of A. In a second embodiment, to rule out or to minimize
factors such as alterations in gastric emptying (e.g., fatty meal, stress, etc.) and/or variable
absorption causing changes in Source 2_A EDIM breath concentrations and causing false
alarms that the active therapeutic drug (A) is not being metabolized properly, a comparator
compound could be included in the pill matrix, which is metabolized by a different enzyme
(location, capacity, and/or function), and would generate another EDIM independent of that
from the active therapeutic drug. For example, lets assume isotope-labeled A is metabolized
by the most important CYP450 enzyme (lower capacity) for drug metabolism, CYP-3A4 to
isotope-labeled A1 (Source 2_A EDIM) whereas the comparator is metabolized by the high
capacity enzyme butyrylcholinesterase to another EDIM. If the ratio of the maximum concentration of the EDIM from the active therapeutic drug to that of the comparator were constant, it is likely the active drug is being metabolized properly. In other words, if the breath isotope-labeled A1 EDIM concentration was reduced, but there is a parallel decrease in the comparator’s EDIM, it would indicate a physiological change such as delayed gastric emptying, which certainly is unrelated to drug metabolism. In contrast, if the ratio markedly changes, it would indicate a potential problem: ratio (A1/comparator) increases - enhanced metabolism of A; versus ratio (A1/comparator) decreases - reduced metabolism of A). Furthermore, like the case in Option 1, the metabolites of the active pharmaceutic, A1 would have the same disadvantages as outlined above.

In another embodiment, by adding different EDIM or combinations of EDIM in addition to those mentioned above, we can conceive of a “genius” level New Intelligent Chemical Entity (NICE) molecule that not only reports its ingestion but also the dose and its metabolism on an ongoing basis. The FDA is highly supportive of improving drug safety. For example, in a recent publication the Center for Drug Evaluation and Research (CDER) stated that the central issue is not whether pharmacogenomic-guided drug prescriptions will happen (Lesko-LJ and Woodcock-J, Pharmacogenomic-guided drug development: regulatory perspective, The Pharmacogenomics Journal (2002) 2, 20–24), but when and where. By ensuring drug adherence and monitoring metabolism with NICE-type drugs, the MAMS technology outlined in this invention will take drug safety to another level.

Moreover, this type of “smart” medication would be naturally the most intelligent at reporting its metabolism, relative to pharmacogenomic-based approaches and/or using enzyme metaprobases (e.g., phenotypic, breath-based tests: $^{14}$C-crythromycin for CYP-3A4, or $^{13}$C-caffeine for CYP-1A2) to elucidate its ability to be metabolized by a given enzyme. Why does this occur? First, blood tests to examine for genetic-based defects in enzyme function (e.g., particular CYP fractions such as 2D6, 2C19 having genetic polymorphisms) only cause problems in a subset of the CYP isoforms and doesn’t involve the most important CYP enzyme, CYP3A4. Second, genetic-based tests ignore an even more important cause of ADRs - drug-drug interactions (DDIs). A patient with a normal genome for a specific enzyme (e.g., normal AmpliChip result being proposed to individualize drug therapy) could be placed on a therapeutic agent that is metabolized by this same enzyme, even though his/her enzyme activity may be actually less than 5% of normal activity due to a DDI! As a
result, he/she may suffer drug-related morbidity and mortality due to a DDI. In a manner being proposed for genetic tests, subjects can be stratified into the following metabolic categories using EDIMs generated from NICE-type therapeutic agents: 1) poor metabolizers, 2) intermediate metabolizers, 3) extensive metabolizers, and 4) ultrarapid metabolizers. Third, many drugs are degraded by multiple enzymatic pathways, including multiple CYP fractions or combinations of CYP and non-CYP enzymes. In many cases it is overly simplistic to focus on the activity of only one enzyme. Thus, genetic tests and breath tests that examine the function of a specific enzyme may not provide an accurate assessment of the net effect (or integrated action) of various degradation pathways and by consequence drug pharmacokinetics and levels. Because many drugs have more than one metabolic route, the EDIMs of smart drugs mentioned in the current invention will not necessarily measure the metabolic rate of any one particular physiological process, but rather identifies and integrates all relevant metabolic pathways in a manner that identifies whether a drug is being properly metabolized in an on-going continuous manner.

If one examines the CYP450 enzyme system, all of the FDA-approved drugs listed in Figures 7-10 have the potential to be converted into "smart" self-reporting (NICE-type) therapeutic molecules. Nevertheless, EDIM Source 2 still limits the system to detecting ingestion of a specific active drug (i.e., one EDIM approach doesn't fill all MAMS needs). Likewise, because so many FDA approved drugs produce common metabolites, particularly formaldehyde via desmethylation reactions (Figure 7), the EDIMs would be similar and may not be able to distinguish among the different therapeutic agents shown in Figure 7. Furthermore, like the case in Option 1, the metabolites of the active pharmaceutic, A1 would have the same disadvantages as outlined above.

In a preferred embodiment, a "genius" level NICE molecule is provided that not only reports its ingestion but also the dose and its metabolism on an ongoing basis. Note: In this application, the use of stable isotopic labeling (e.g., deuterium) to generate EDIMs, should have minimal-to-no impact on chemistry-manufacturing controls (CMC) or active pharmaceutical ingredients (API), and thus should invoke minimal regulatory scrutiny.

In another embodiment, the technology described in the current application could be used to provide a new and novel basis, independent of existing technologies (e.g., scintigraphic tests that scan the stomach with radiographic equipment, or breath-based C-octanoate tests that measure expired CO2 with expensive analytical devices), of non-
invasively measuring gastric emptying using ordinary and non-ordinary isotopic-labeled EDIM(s) and a sensor to measure them. The test would simply require a subject to exhale breath into a sensor for a short period of time at intermittent times, immediately before and after ingesting a pill. For example, consider a pill system, which contains 3 key chemical design elements, that will interface with a sensor to measure the concentration of EDIMs in the breath: 1) “mouth” chemicals to “time stamp” entry of the pill system into the mouth, 2) “stomach” chemicals to “time stamp” entry of components of the pill system into the stomach, and 3) “small intestine” chemicals to “time stamp” entry of components of the pill system into the small intestine.

**Mouth Chemicals:** Mouth chemicals surface coated on (one preferred embodiment) or located within the pill (e.g., including but not limited to a gelatin capsule) will immediately generate a mouth-derived EDIM(s), either derived directly from the mouth chemical(s) (preferred embodiment), metabolites of the mouth chemicals, or both, upon entry into the mouth and will thus “time stamp” when the pill was placed into the mouth.

**Stomach Chemicals:** Stomach chemicals surface coated or contained within (one preferred embodiment) the pill (e.g., including but not limited to a gelatin capsule) will be quickly released from the capsule (preferred embodiment) and be significantly absorbed into the blood via transport through the gastric wall (e.g., includes but not limited to ethanol) and will be immediately detected as a stomach EDIM and/or stomach EDIMs, either by measuring the stomach chemical(s) themselves, metabolite(s) of the stomach chemical(s) via enzyme action (preferred enzyme is located in blood and high capacity to rapidly generate the stomach EDIMs), or combinations of both. Thus, the appearance of stomach chemical-derived EDIMs will “time stamp” entry of the pill system into the stomach.

**Small Intestine Chemicals:** Small intestine chemicals coated on or contained within (preferred embodiment) the pill (e.g., including but not limited to a gelatin capsule) is a chemical or more than one chemical, hereafter called the “small intestine” chemical, that is absorbed into the blood via transport through the wall of the small intestine, preferably through the duodenum, but not through the wall of the stomach; shortly after entering the small intestine and entering the blood stream, the small intestine chemical(s) will be immediately detected as a small intestine EDIM and/or small intestine EDIMs, either by measuring the small intestine chemical(s) themselves, metabolite(s) of the small intestine chemicals via enzyme action (preferred enzyme is located in blood and high capacity to
rapidly generate the small intestine EDIMs), or combinations of both. Thus, the appearance of small intestine chemical-derived EDIMs will "time stamp" entry of the pill system into the small intestine. The use of the mouth, stomach and small intestine "time stamps" described above, unlike current systems used to measure gastric emptying, will allow not only gastric emptying times to be measured non-invasively, but also allow simultaneous assessment of esophageal transit times and subsequent correction of gastric emptying times (subtracting off esophageal transit time). A number of medical conditions and/or drugs can affect esophageal transit and gastric emptying independent of one another. In addition, the described system could be further expanded to assess emptying times at other elements of the gastrointestinal tract, such as the colon where bacteria can be used to liberate unique colon EDIMs. In all of these applications, the pill system can be administered under various conditions, including fasting, standard liquid meal and/or standard fatty meals.

**Option 3:** EDIM Source 1_S - Detection of S: The major limitation of Option 3 is that MAMS would be designed to detect a single salt, S as the EDIM that is chemically part of the active therapeutic agent, A. This approach may or may not suitable for MAMS. A second disadvantage is that the physicochemical characteristics, pharmacokinetics or effective therapeutic concentrations of a salt may not be suitable for detection in the breath. One illustrative example for Option 3 would be isotopic (e.g., \(^{13}\text{C}, \, ^{17}\text{O}, \, ^{18}\text{O}\) and/or deuterium)-labeled acetate (acetic acid), which is frequently used as a pharmaceutical salt, and is quite volatile and may serve as a Source 1_S EDIM.

**Option 4:** EDIM Source 2_S - Detection of S1: Option 4 (detection of the major metabolites of S, S1 in the breath post oral ingestion) may also be feasible in some embodiments. For example, acetate (acetic acid) was mentioned in Option 3. Isotope (e.g., \(^{13}\text{C}, \, ^{17}\text{O}, \, ^{18}\text{O}\) and/or deuterium from Table 2)-labeled acetic acid (Figure 6) is converted to \(\text{CO}_2\) and \(\text{H}_2\text{O}\) via the tricarboxylic acid (TCA) cycle. These metabolic products, containing isotopic-labels, could serve as a Source 2_S EDIM.

As shown in Figure 7, many therapeutic agents directly generate formaldehyde via desmethylation reactions. In terms of assessing metabolic function, such as CYP activity, the production of formaldehyde, rather than \(\text{CO}_2\), is a more accurate measure of metabolic function. By using \(\text{CO}_2\) as the breath marker to assess enzyme competence, two additional enzyme systems (Figure 6) are brought into the picture (i.e., alcohol dehydrogenase, formaldehyde [aldehyde] dehydrogenase). If a defect in either enzyme system was present, it
is possible to falsely conclude that CYP function was abnormal, versus a defect in the enzyme(s) system distal to formaldehyde. As confirmation of this problem, because the production of carbon dioxide from the oxidation of many CYP-substrates such as erythromycin is folate-dependent (Figure 6), a reduction in the folate-dependent intermediate step caused an abnormal test in the erythromycin breath test, when in reality no metabolic abnormality was found in CYP-3A4 function. The technology outlined in this application, particularly in reference to the NICE concept, may be able to exploit the use of isotopic-labeled formaldehyde (or any other aldehyde, etc) in order to directly measure CYP activity and thus avoid this potential pitfall, and provide a basis for drugs that self report their metabolism.

**Option 5:** EDIM Source 1_E - **Detection of E:** Many excipients (Table 5) exist that are used to optimize formulation of a therapeutic agent. Some of these agents may be suitable to provide isotopic-label Source 1_E EDIMs for MAMS.

**Option 6:** EDIM Source 2_E - **Detection of E1:** Isotopic-labeled EDIMs arising from excipients also may be used for MAMS. For example, aspartame or neotame are an ester-based artificial sweetener that liberates L-phenylalanine, aspartic acid and methanol when it is hydrolyzed.

**Option 7:** EDIM Source 3 - **Detection of T:** The presence of T may not be necessary if the EDIM can be generated by other sources. The major advantage of Option 7 (detection of T which is ingested along with a capsule containing A) is that it not only allows the selection of a chemical taggant that possesses the attributes of the ideal EDIM (see Section B.4 for details), but also it can be utilized to verify oral ingestion of *any* active pharmacuetic. However, by utilizing T, rather than a metabolite of T, T1 (Option 8), we cannot guarantee that the tablet was ingested. This drawback can be significantly mitigated or even eliminated by pill design factors.

**Option 8:** EDIM Source 4 - **Detection of T1:** In this approach for isotope-based MAMS (detection of isotope-labeled T1 as the EDIM), A and T co-exist in the same pill/capsule but in the preferred embodiment the presence of T does not alter the CMC/API of the active pharmaceutical ingredient. It has 3 major advantages: 1) allows the selection of a chemical taggant that possesses the attributes of the ideal EDIM (see Section B.4. for details), 2) can be utilized to verify oral ingestion of *any* active pharmacuetic, and 3) can guarantee that the active pharmacuetic was ingested, entered the blood, traveled to its biological target sites and
via its mechanism(s) underlying efficacy exerted its therapeutic action. For example, if an enzyme which is located in the liver converts T to T1, then detection of T1 in the breath definitively confirms pill/capsule ingestion of active drug in the person who actually put the tablet in their mouth.

Preferred Isotopic-labeled EDIM for MAMS

Independent of the source of the EDIM (see four general sources of EDIMs above), at least 12 factors should be considered when designing a system to generate the ideal EDIM for an effective MAMS:

1. Applicable to all oral administration regimens. Although the oral route is the preferred embodiment, other routes of administration may include but are not limited to non-oral routes such as intravenous, transdermal, rectal, nasal, cerebrospinal fluid, subcutaneous, intramuscular).

2. Reproducible, rapid appearance of the EDIM in breath after ingestion and absorption of the pill.

3. Reproducible duration of EDIM appearance in the breath for QD or BID dosing: duration is not greater than 5 hrs or less than 15 min.

4. The EDIM is unique in the breath (e.g., not found in multiple foods, not found normally during endogenous metabolism, and not produced in high concentration during disease) and provides a good signal to noise ratio with the detector.

5. Type of metabolism not critical but if T is used to generate the EDIM, it is preferably non-CYP (e.g., esterase) to avoid potential drug-drug interactions (DDIs); a “smart” drug has the potential to not only generate an EDIM to confirm medication adherence but also self reports it metabolism.

6. EDIM is relatively volatile to readily appear in the breath but not extremely evanescent in the blood; does not undergo very fast subsequent metabolism to nonvolatile metabolites. Ideally, the EDIM should not have a pKa value that renders the majority of the molecule to the charged state at physiological pH (pH = 7.4), which may poorly appear in the breath.

7. Has no intrinsic toxicity, pharmacological activity, or inhibitory effect on the metabolism of other compounds at concentrations required for detection. For example, subjects on disulfiram, which inhibits aldehyde dehydrogenase and causes acetaldehyde to
accumulate (development of “flu-like symptoms” in humans is a negative incentive to consume alcohol), is used to treat alcoholism and may cause an aldehyde-based EDIMs to produce side effects due to higher than expected levels of the aldehyde). This scenario is very unlikely given the low dose of taggants used to generate the EDIM in MAMS, and the concentrations of EDIM formed for MAMS applications.

8. EDIMs may be of any or combination of the 3 drug classes described in Section A.

9. Ideal EDIMs should be stable in the body, be exclusively eliminated by exhalation, and not undergo additional metabolism. This criterion will almost never be met with GRAS type taggants.

10. If a tagnant is used to generate the EDIM, it should not alter the PK/PD of the therapeutic agent (e.g., API has bioequivalence; API has the same biological interaction with the body, and ADME).

11. The chemical source of the EDIM should be inexpensive, readily available, and easy to synthesize.

12. The formation of the EDIM should not be easily blocked by other chemicals (e.g., therapeutic agents or non-therapeutic chemicals that inhibit the enzyme that liberates the EDIM) or pathophysiological conditions frequently present in humans.

Additional selection criteria for taggants in MAMS, which may be used to generate the EDIM, include: 1) state of matter: solid versus liquid; 2) taste: absent or present (pleasant vs unpleasant); 3) physicochemical properties: boiling point, melting point, Henry’s Law constant (K_H); 4) PK properties: ADME, including metabolism rates and routes (non-CYP-450 to avoid adverse drug reactions [ADRs]); 5) extensive safety data: stability, toxicological data such as permissible daily exposure (PDE) in humans and LD_50 values in various species (typically in the gms/kg range for oral administration); 6) minimal-to-no implications from a regulatory perspective (no impact on CMC of API [study drug or FDA approved drug] or PK/PD of API); and 7) metabolism of tagnant generates EDIMs that are easily detected by the appropriate detection technologies (e.g., IR) (e.g., EDIM is detected by the sensor and is neither a significant endogenous chemical nor widely generated via ingestion of different foods).

Enzyme Chemistry, EDIMs and MAMS
To generate isotopic-labeled EDIMs via catalysis that are suitable for MAMS, a great diversity of Class 1, 2, and/or 3 drugs (described above) exist that can be acted upon by several types of enzymes. A carboxylate ester, when acted upon by an esterase(s), liberates an acid and alcohol (Figure 1). In the case of many GRAS ester taggants, the metabolites, namely an alcohol (Figure 2) and a carboxylic acid (Figure 3) can be selected as EDIMs because one or both can be volatile (or semivolatile) and thus serve as EDIMs. In addition, carbonate esters, acetals and ketals can also be used to easily generate a wide variety of corresponding alcohols and carboxylic acids as EDIMs. The 1° and 2° alcohols, generated from these compounds, will in turn, generate aldehydes and ketones, respectively. The aldehydes, and particularly the ketones may also be suitable EDIMs.

Compared to carboxylic acids, alcohols are a more suitable EDIM for a variety of reasons (e.g., carboxylic acids have poor [high] K_H values (=CL/CIG, liquid to gas phase concentration ratio that cause them to partition preferably in blood versus breath). In the case of 1° alcohol-based aliphatic esters (1° esters) such as ethyl butyrate, esterases rapidly create a 1° alcohol (i.e., ethanol). For 2° alcohol-based aliphatic esters (2° esters) such as 2-pentyl butyrate, they are rapidly hydrolyzed to their corresponding 2° alcohol (i.e., 2-pentanol) by esterases, particularly by carboxylesterases (e.g., β-esterase). The carbon that carries the hydroxyl (-OH) group of primary (1°), secondary (2°) and tertiary (3°) alcohols is attached to 1, 2, and 3 alkyl groups, respectively. The 1° and 2° alcohols are primarily converted (oxidized) via alcohol dehydrogenase (ADH) to their corresponding aldehydes and ketones, respectively. In contrast to 1° and 2° alcohols, 3° alcohols, due to steric hindrance with ADH, are very resistant to metabolism in humans and thus are not ideal for MAMS, unless a 3° alcohol-based ester liberated a 3° alcohol (e.g., tert-butyl butyrate to tert-butanol), which was used as the EDIM. The aldehydes are further metabolized by aldehyde dehydrogenase (ALDH), which oxidizes (dehydrogenates) them to their corresponding carboxylic acid. In contrast, methyl ketones undergo α-hydroxylation (e.g., conversion of 2-butanol [methyl ethyl ketone, MEK] to 3-hydroxy-2-butanone [acetoin] via CYP-2E1 and CYP-2B, or conversion of 2-pentanone [methyl propyl ketone, MPK] to 3-hydroxy-2-pentanone) and subsequent oxidation of the terminal methyl group to eventually yield corresponding ketocarboxylic acids. Unlike aldehydes, disulfiram (an inhibitor of ALDH) should not inhibit the metabolism of ketones. The ketoacids are intermediary metabolites (e.g., α-ketoacids) that undergo oxidative decarboxylation to yield CO2 and simple aliphatic carboxylic acids.
The acids may be completely metabolized in the fatty acid pathway and citric acid cycle.

It appears that $2^\circ$ alcohols (or even $2^\circ$ esters that generate $2^\circ$ alcohols) are excellent taggants for definitive adherence monitoring, and appear superior to the simple $1^\circ$ alcohols in this respect. The presence (and persistence) of their corresponding ketones (EDIMs) in exhaled breath represents definitive proof of ingestion of a medication containing $2^\circ$ alcohols (or a $2^\circ$ alcohol-based ester, carbonate ester, ketal, etc.) as taggants. In general due to increased steric hindrance, $2^\circ$ alcohols are not as good substrates for ADH relative to $1^\circ$ alcohols. Likewise, the enzymatic pathways to degrade alcohol-derived ketones appear less efficient than those for alcohol-derived aldehydes. Given the fact that 1) the gastric wall has a high concentration of ADH and alcohols (e.g., ethanol) are known to be significantly absorbed through the stomach, and 2) alcohols undergo extensive first pass metabolism via ADH in the liver after absorption from the GI tract, it should not be surprising that 2-butanone levels appear very rapidly in the breath, and its concentrations significantly exceeds those of 2-butanol (ketone:alcohol ratio: 2-butanone/2-butanol $\gg$1).

In addition, other $2^\circ$ alcohols will increase the number of taggants available for definitive adherence monitoring. In keeping with our hypothesis that $2^\circ$ alcohols (vis-à-vis $1^\circ$ alcohols) would generate ketones that would persist in the body and have significant excretion by the lung, diabetic patients readily excrete ketones during the pathophysiological condition of diabetic ketoacidosis (DKA). Therefore, it should not be surprising that ketones generated from other sources (e.g., orally ingested $2^\circ$ alcohols) would also be excreted by the lung. Using mGC-MOS we have already shown these endogenous DKA-related ketones are easily distinguished from the ketones, which would be generated from $2^\circ$ esters or alcohols, including 2-butanone and 2-pentanone (data not shown).

Below is a summary of some key advantages and disadvantages of using esters, $1^\circ$ alcohols and $2^\circ$ alcohols for definitive MAMS:

A. Esters

Advantages

- Great variety of GRAS food additives
- Esterases generate corresponding alcohol and carboxylic acid via enzyme systems that are widely present in humans and not easily saturable
- Many exist in liquid and solid state forms
- Relative to alcohols, many more choices for selecting solids
- Great variety of favorable tastes
- $2^\circ$ alcohol-based esters such as 2-pentyl butyrate are primarily degraded by carboxylesterase to 2-pentanol and butyric acid

**Disadvantages**

- Greater mass of taggant required to be interfaced to API in order to generate a fixed mass of EDIM (e.g., 2-butanone)
- Some esters not optimal from a stability standpoint
- $1^\circ$ alcohol-based esters as GRAS compounds are much more common than $2^\circ$ alcohol-based esters in food databases; these alcohols generate aldehydes, which are not ideal EDIMs relative to ketones derived from $2^\circ$ alcohols

**B. $1^\circ$ alcohols**

**Advantages**

- Much greater variety of GRAS food $1^\circ$ alcohols relative to $2^\circ$ alcohols
- Larger $1^\circ$ alcohols via ADH generate aldehydes, particularly those that are branched, which are better EDIMs (e.g., low KH values; distinct from endogenous compounds) than more simple $1^\circ$ alcohols, but have lower vapor pressures

**Disadvantages**

- ADH forms aldehydes from $1^\circ$ alcohols, which are generally not as good EDIMs as ketones, particularly with the more simple $1^\circ$ alcohols
- Many have classic alcohol taste; may require CMC architecture approaches or addition of taste "maskers" to avoid
- Disulfiram, a drug used to treat alcoholism that blocks the action of aldehyde dehydrogenase, may interfere with the degradation of corresponding aldehydes, and cause side effects; this effect is expected to be clinically irrelevant due to the small mass of alcohol (or its corresponding ester) required for definitive MAMS
- Ethanol consumption (via interaction with ADH) can theoretically reduce the conversion of
1° alcohol tagant to its corresponding aldehyde; this has not been found to be clinically significant for a number of non-ethanol alcohols (excludes methanol).

Note: In addition of 1o alcohols, a number of critically important CYP-450 metabolic reactions for pharmaceutical agents, via dealkylations, generate various aldehydes, include formaldehyde via demethylation, acetaldehyde via desmethylation, propionaldehyde via despropylation, and butyraldehyde via desbutylation.

C. 2° alcohols

Advantages
- ADH generates ketones, which generally have more favorable physicochemical and metabolism characteristics as EDIMs than aldehyde ones
- Disulfiram, an inhibitor of aldehyde dehydrogenase, will not interfere with the degradation of ketones formed from 2o alcohols (e.g., methyl ethyl ketone, derived from 2-butanol, is converted to 3-hydroxy-2-butanone via CYP-2E1 and 2B).

Disadvantages
- Many have classic alcohol (ethanol) taste; may require CMC architecture approaches or addition of taste “maskers” to avoid
- Few 2° alcohols, relative to 1o alcohols, are listed in GRAS food databases
- Few 2° alcohol-based esters are listed in GRAS food databases (e.g., these would generate the 2° alcohol, and later a ketone)

Because esterases (unlike the CYP450 system) are high capacity enzyme systems, their exploitation for MAMS is desirable, as the presence of ester taggant(s), if used and necessary, is not likely to cause drug-drug interactions (DDIs) or have its function in MAMS be adversely impacted by DDIs, when co-administered with therapeutic agents.

The vast majority of pharmaceutics are metabolized by CYP450 (Figure 4 lists some key P450 reactions), particularly CYP-3A4 and CYP-2D6. Likewise, the redundancy of various esterase functions in humans (a drug can be metabolized by different esterases) is desirable to avoid the impact of genetic alterations in enzyme function (e.g., genetic polymorphisms with CYP-2D6, CYP-2C9 and/or CYP-2C19) that could adversely impact a
MAMS system using CYP-based taggant substrates. On the other hand, in the case of NICE-type drugs that are metabolized by the CYP450 system, when the active therapeutic “self reports” not only its ingestion but also its metabolism, it is of course desirable and necessary in this situation for the EDIM to be derived from the CYP450 enzyme system, in order for the drug to be “smart”.

The breath kinetics (presence, rapidity of appearance, concentration, duration of presence, etc) of the isotope-labeled EDIM(s) is a function of the following factors: 1) dose of Class 1, 2 or 3 drug(s) used as the EDIM(s) or generating the EDIM(s) (via enzymatic action), 2) the rate of liberation of the EDIM(s) via enzyme action into the blood, 3) rate of removal of the EDIM via non-breathe endogenous metabolic routes (e.g., conversation of alcohols, aldehydes and carboxylic acids generated by enzymes such as esterases or CYP450 to CO₂ and H₂O via the TCA cycle; see Figure 2) and 4) intrinsic EDIM properties (e.g., physicochemical properties such as vapor pressure and pharmacokinetic features such as metabolic half life, clearance, volume of distribution, pKa).

Many of the EDIMs, which have suitable physicochemical properties (e.g., volatility, duration of appearance in breath, etc.) for MAMS, are already present in the blood and breath of humans as part of endogenous metabolism and/or diet. This applies to a variety of chemically diverse substances, including but not limited to alcohols, fatty acids, aldehydes, ketones. For example, in humans the endogenous blood and breath concentrations of ethanol, methanol and formaldehyde are shown below:


Methanol is thought to be formed from the microflora of the gastrointestinal tract and from dietary intake. Methanol may not be suitable for MAMS due to the effects of ethanol on completely or nearly completely blocking methanol oxidation. Ethanol is the preferred substrate of alcohol dehydrogenase and its presence in the blood after imbibing ethanol will
markedly lengthen the half life of methanol in the body. For example, methanol has a half life in the blood in the absence of alcohol of 1.8-3.0 hrs versus greater than 8-24 hrs in the presence of alcohol (Haffner et al, Int J Legal Med, 105:111-114, 1992), making it potentially unsuitable as an EDIM. The half life of the EDIM has to be short enough so its presence does not interfere with subsequent dosing, which is obviously more of a problem with drugs given more than once per day. A number of other volatiles resulting from endogenous metabolism can also be found in human breath. For example in one study (Diskin-AM et al, Physiol Meas 24:107-119, 2003), the mean concentrations, in parts per billion (ppb), for the listed compounds were: ammonia, 422–2389; acetone, 293–870; isoprene, 55–121; ethanol, 27–153; acetaldehyde, 2–5. If the above molecules contained only ordinary isotopes and were proposed as EDIMs, it may be difficult in many cases to distinguish them from background levels (poor signal to noise ratio), and thus they would not be ideal for MAMS application. In contrast, if we used non-ordinary isotope-labeled EDIMs, these entities can be readily distinguished from the endogenous compounds on the basis of various techniques, including but not limited to infrared spectroscopy (see Figures 11-27) or mass spectroscopy.

Examples of appropriate infrared spectrometers include but are not limited to those disclosed in U.S. Patent 5,063,275, herein incorporated by reference. For example, to illustrate this concept, if deuterated (or carbon labeled) formaldehyde could be readily discriminated from endogenous (background) formaldehyde and if enough labeled formaldehyde, when liberated via CYP-mediation oxidation of the parent compound, can escape the metabolic machinery of cells (conversion of formaldehyde to formic acid and CO₂, Figure 6) and flow into the blood, this would allow medication adherence and even the metabolism to be monitored of many, if not all, of the FDA-approved drugs listed in Figure 7. On the other hand, if this turns out not to be the case and given the fact that the CYP system is easily saturable and frequently causes ADRs (and morbidity and mortality) due to DDIs and genetic abnormalities, the current invention may provide an impetus for pharmaceutical companies to create new chemical entities that are degraded by non-CYP450 (preferred embodiment) but also by CYP450 pathways to generated EDIMs, which allow for the molecule to be “smart” (i.e., it would self report adherence and metabolism).

Although the Katzman technology (United States Patent 5962335) teaches how to predict using isotope breath tests whether a drug will be properly metabolized by a subject prior to being placed on that particular drug (proposed individualized therapy), the invention
described herein differs in many important respects. First, Katzman does not teach how to
use isotopic labeling for purposes of assessing medication adherence, including frequency of
drug dosing and dosage of a medication. Second, we propose to invent a new class of
therapeutic agent, termed “smart drugs” or NICE-type agents, which continuously monitors
not only medication adherence, but also its ability to metabolize themselves in a continuous
manner. Thus, in the preferred embodiment we propose continuous monitoring and not a
single a priori assessment of metabolic competence before being placed on the medication,
which is the approach taken by Katzman. It is likely that most ADRs, such as DDIs or
physiological abnormalities would occur while on drug therapy, particularly for those drugs
which are taken over a patient’s lifetime. Third, the actual physical material of active
therapeutic agent that is being used to assess metabolic competence is actually being used to
treat the patient’s medical disorder. In other words, our invention will preferably use the
active therapeutic drug itself when it is being actually used to treat disease to simultaneously
monitor its own metabolism, as opposed to the Katzman approach of using an exogenously
administered test drug probe (the drug here is not being used to treat medical disorders) to
assess metabolic competence. The principal of NICE type agents, where a fragment of the
parent FDA approved drug, can be used to assess medication adherence and metabolism,
while it is simultaneously treats disease, is completely novel. Fourth, Katzman proposes to
use the most distal products of metabolism, such as labeled CO₂ and NH₃, but does not
explicitly mention the use of more proximal ones, including but not limited to alcohols, acids,
aldehydes, and/or ketones, which is a preferred embodiment of the current invention. Fifth,
Katzman does not explicitly mention the use of deuterium, which is a preferred embodiment
as an isotopic label for EDIMs. In summary, unlike the current invention, it was not intent of
Katzman to create a new class of “smart” therapeutics agents, based on selective isotopic
(preferably non-radioactive, Table 2) labeling that does not alter the active drug’s PK/ADME
or pharmacodynamics, which is given chronically (or acutely) to treat disease while
simultaneously and continuously monitoring adherence and metabolism.

Illustrative Examples of How Isotope-labeled EDIMs Can Be Enzymatically Generated from
Class 1, 2, and 3 Drugs

As outlined above, a number of strategies can be used to create a variety of flexible
medication adherence systems (MAMS), some of which may involve chemistry that will
allow the therapeutic molecules to be "smart" since they will treat disease while simultaneously monitoring adherence and metabolism. In this section, we describe 3 enzyme systems, namely esterases, CYP450 and deaminases, which can generate isotopic-labeled EDIMs. Each enzyme will be following by selected illustrated examples of how Class 1, 2 and 3 drugs can be used in MAMS. Note: In most cases, the parent molecule will be broke down in a smaller more volatile fragment(s), which is the preferred embodiment for the EDIM(s), but does not exclude using the larger metabolic fragment(s) as an EDIM(s).

**Esterases**

Esters (EC 3.1.1) are hydrolyzed without the requirement of molecular oxygen by esterases to a carboxylic acid and an alcohol (Figure 1). Esterases, hydrolases which split ester bonds, hydrolyze a number of compounds used as drugs in humans. The enzymes involved are classified broadly as cholinesterases (including acetylcholinesterase), carboxylesterases, and arylesterases, but apart from acetylcholinesterase, their biological function is unknown. The acetylcholinesterase present in nerve endings involved in neurotransmission is inhibited by anticholinesterase drugs, e.g. neostigmine, and by organophosphorous compounds (mainly insecticides and chemical warfare agents). Cholinesterases are primarily involved in drug hydrolysis in the plasma, arylesterases in the plasma and red blood cells, and carboxylesterases in the liver, gut and other tissues. By incorporating various isotopic labels listed in Table 2 (preferred embodiment is deuterium), where appropriate, into the various atomic sites of the esters, various EDIMs (arising from the ester, acid and/or alcohol, and their corresponding ketone/aldehyde) containing one or more isotopic labels could be generated that will fulfill the requirements of an effective MAMS.

Below are nine examples (Figures 29-37) of how different Class 1, 2 and 3 molecules could be isotopically labeled for MAMS:

**Ester Example 1:** Aspartame – Figure 29. Aspartame is a food additive, considered GRAS by FDA; artificial sweetener. It mimics the taste of sugar in humans. It is rapidly metabolized by human gut esterases and gut peptidases in humans. Its metabolites consist of L-aspartic acid + L-Phenylalanine + Methanol. According to the subject invention, the NICE Embodiment – Chemical Group Site(s) of Isotopic Label(s) on Parent Molecular Structure:
Preferred site is the methyl group on Aspartame (indicated by circle) but may include other locations on the parent molecule. In another embodiment of the invention, the NICE Embodiment – Type of Isotopic Labeling onPreferred Site(s): insertion of isotopic label(s) on the preferred site, including but not limited to a) a single label of a given isotope type (e.g., one Deuterium label = CDH2) on the preferred site(s), b) multiple labels of a given isotope (e.g., greater than one deuterium = CD2H or CD3) on the preferred site(s), or c) combinations of different types and numbers of isotopes (e.g., deuterium, carbon and/or oxygen = 13CDH2, 13CHD2, or 13CD3) on one or more locations of the preferred site(s). In yet another embodiment of the invention, the NICE Embodiment – Preferred Labeled Entity for Detection: isotopic (e.g., deuterium) labeled methanol in the breath; a less preferred embodiment would be labeled metabolic products of methanol (formaldehyde, formic acid and/or CO2 - see Figure 6 for details of metabolism of methanol). Isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

Ester Example 2: Acetylsalicylic Acid – Figure 30. Acetylsalicylic Acid is an over the counter (OTC) drug. It is a nonsteroidal anti inflammatory drug (NSAID) that irreversibly inhibits cyclooxygenase (COX) via acetylation of the serine residue at the active site of COX, which suppresses production of prostaglandins and thromboxanes. It is metabolized by Acetylsalicylic Acid (ASA) esterases in humans. It metabolites consist of 2 acids (salicylic acid and acetic acid). In one embodiment, the NICE Embodiment – Chemical Group Site(s) of Isotopic Label(s) on Parent Molecular Structure: Preferred site is the methyl group on ASA (indicated by red circle) but may include other locations on the parent molecule. In another embodiment, the NICE Embodiment – Type of Isotopic Labeling on Preferred Site(s): NICE Embodiment – Type of Isotopic Labeling on Preferred Site(s): insertion of isotopic label(s) on the preferred site, including but not limited to a) a single label of a given isotope type (e.g., one Deuterium label = CDH2) on the preferred site(s), b) multiple labels of a given isotope (e.g., greater than one deuterium = CD2H or CD3) on the preferred site(s), or c) combinations of different types and numbers of isotopes (e.g., deuterium, carbon and/or oxygen = 13CDH2, 13CHD2, or 13CD3) on one or more locations of the preferred site(s). In yet another embodiment, the NICE Embodiment – Preferred Labeled Entity for Detection: isotopic (e.g., deuterium) labeled acetic acid in the breath; a less preferred embodiment would be labeled metabolic products of acetic acid, CO2 - see
Figure 6 for details of metabolism of acetic acid). Isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

Ester Example 3: Parabens – Figure 31. Paraben is an abbreviation for para-hydroxybenzoic acid. Parabens are a family of alkyl esters of para-hydroxybenzoic acid that differ at the para position of the benzene ring. There are four widely marketed para-hydroxybenzoic acid (POHBA) esters: methylparaben, ethylparaben, propylparaben, and butylparaben. Used as food additives/preservatives; considered GRAS by FDA; Europe uses as ADI (acceptable daily intake) up to 10 mg/kg per day for methyl and ethyl paraben. It inhibits bacterial growth; food additive. It is rapidly metabolized by carboxylesterases and tissue esterases in humans. Its metabolites consist of para-hydroxybenzoic acid (POHBA) + corresponding alcohol (see below for details). In one embodiment, the NICE Embodiment – Chemical Group Site(s) of Isotopic Label(s) on Parent Molecular Structure: Preferred site is the methyl group on Aspartame (indicated by red circle) but may include other locations on the parent molecule. In another embodiment, the NICE Embodiment – Type of Isotopic Labeling on Preferred Site(s): insertion of isotopic label(s) on the preferred site, including but not limited to a) a single label of a given isotope type (e.g., one Deuterium label = CDH2) on the preferred site(s), b) multiple labels of a given isotope (e.g., greater than one deuterium = CD2H or CD3) on the preferred site(s), or c) combinations of different types and numbers of isotopes (e.g., deuterium, carbon and/or oxygen = 13CDH2, 13CHD2, or 13CD3) on one or more locations of the preferred site(s). In yet another embodiment, the NICE Embodiment – Preferred Labeled Entity for Detection: isotopic (e.g., deuterium) labeled alcohols in the breath; a less preferable embodiment is labeled distal metabolic products of the alcohols and acids generated from the different parabens (see Figure 6 for details). Isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

Ester Example 4: Clofibrate – Figure 32. Clofibrate is a prescription medication. It is a hypolipidemic drug, known to induce peroxisome proliferation; a member of a large class of diverse exogenous and endogenous chemicals known as peroxisome proliferators; Activation of the peroxisome proliferator activated receptor- (PPAR-α) key aspect of efficacy,. It is metabolized by human esterases. Its metabolites consist of carboxylic acid
derivatives of Clofibrate + Ethanol. In one embodiment, the NICE Embodiment – Chemical Group Site(s) of Isotopic Label(s) on Parent Molecular Structure: Preferred site is the ethyl group on clofibrate, particularly on the methyl group (indicated by red circle) but may include other locations on the parent molecule. In another embodiment, the NICE Embodiment – Type of Isotopic Labeling on Preferred Site(s): insertion of isotopic label(s) on the preferred site, including but not limited to a) a single label of a given isotope type (e.g., one Deuterium label = CH2CH2D) on the preferred site(s), b) multiple labels of a given isotope (e.g., greater than one deuterium = CH2CHD2, CH2D3, CHD2D3, CD2CD3) on the preferred site(s), or c) combinations of different types and numbers of isotopes (e.g., deuterium, carbon and/or oxygen on one or more locations of the preferred site(s). In yet another embodiment, the NICE Embodiment – Preferred Labeled Entity for Detection: isotopic (e.g., deuterium-based) labeled ethanol in the breath; a less preferred embodiment would be labeled metabolic products of ethanol (acetaldehyde, acetic acid and/or CO2 - see Figure 6 for details of metabolism of ethanol). Isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

Ester Example 5: Esmolol – Figure 33. Esmolol is a controlled/prescription drug. It is an ester-based ultra short acting beta blocker that is beta1 receptor selective. In contrast to most ester-containing drugs, the hydrolysis of esmolol is mediated by an esterase in the cytosol of red blood cells (RBC) called arylesterase. Its metabolites consist of carboxylic acid derivatives of Esmolol + Methanol. In one embodiment, the NICE Embodiment – Chemical Group Site(s) of Isotopic Label(s) on Parent Molecular Structure: Preferred site is the methyl group on esmolol (indicated by red circle) but may include other locations on the parent molecule. In another embodiment, the NICE Embodiment – Type of Isotopic Labeling on Preferred Site(s): NICE Embodiment – Type of Isotopic Labeling on Preferred Site(s): insertion of isotopic label(s) on the preferred site, including but not limited to a) a single label of a given isotope type (e.g., one Deuterium label = CDH2) on the preferred site(s), b) multiple labels of a given isotope (e.g., greater than one deuterium = CD2H or CD3) on the preferred site(s), or c) combinations of different types and numbers of isotopes (e.g., deuterium, carbon and/or oxygen = 13CDH2, 13CHD2, or 13CD3) on one or more locations of the preferred site(s). In yet another embodiment, the NICE Embodiment – Preferred Labeled Entity for Detection: isotopic (e.g., deuterium) labeled methanol in the
breath; a less preferred embodiment would be labeled metabolic products of methanol (formaldehyde, formic acid and/or CO2 - see Figure 6 for details of metabolism of methanol). Isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

Ester Example 6: Procaine – Figure 34. Procaine is a prescription drug. It is a local anesthetic for nerve conduction blocks; blocks sodium (Na+) channels. It is metabolized in humans by human pseudocholinesterase (butyrylcholinesterase). Its metabolites consist of carboxylic acid derivatives of procaine (para-aminobenzoic acid) + 2-(Diethylamino)-ethanol. In one embodiment, the NICE Embodiment – Chemical Group Site(s) of Isotopic Label(s) on Parent Molecular Structure: Preferred site is one or both ethyl groups on procaine, preferentially located on the methyl (ethyl group indicated by red circle) but may include other locations on the parent molecule. In another embodiment, the NICE Embodiment – Type of Isotopic Labeling on Preferred Site(s): insertion of isotopic label(s) on the preferred site, including but not limited to a) a single label of a given isotope type (e.g., one Deuterium label = CH2CH2D) on the preferred site(s), b) multiple labels of a given isotope (e.g., greater than one deuterium = CH2CHD2, CH2D3, CHDCD3, CD2CD3) on one or two ethyl groups as the preferred site(s), or c) combinations of different types and numbers of isotopes (e.g., deuterium, carbon, nitrogen and/or oxygen on one or more locations of the preferred site(s). In yet another embodiment, the NICE Embodiment – Preferred Labeled Entity for Detection: isotopic (e.g., deuterium-based) labeled 2- (Diethylamino)-ethanol in the breath. Isotopic labeling of larger metabolic fragments (e.g., PABA) derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

Ester Example 7: New Chemical Entity – Cyclic Molecule Containing 3 Ester Bonds – Figure 35. Figure 35 illustrates an ester-based cyclic NCE that can generate 3 different alcohols (ethanol, n-propanol, and tert-butanol) as EDIMs. Each of the 3 ester bonds on the NCE will be hydrolyzed and release a carboxylic acid(s) and 3 different alcohols. At least 3 major advantages exist for creating these types of NCEs for MAMS applications: 1) it allows custom-designed patterns of EDIMs to be released via enzymes (either a single type or more than one type) that can provide excellent discrimination (e.g., combination of EDIMs in breath is highly distinctive and can be used to eliminate the effect of diet or disease on
MAMS function), 2) different combinatorial permutations (e.g., a single NCE containing one or more ester groups versus combinations of different NCEs, each containing one or more distinctive ester groups) of these types of molecules can be used to isotopically and/or non-isotopically label different dosage forms of a given drug (e.g., warfarin) and/or multiple types of different medications, and 3) by combining distinctive EDIMs into a NCE, the mass of drug (preferred embodiment is the solid form) required to release these patterns of EDIMs can be minimized. The latter is important because mass limitations in a pill matrix for MAMS will exist. For example, for the NCE shown above (MW=336.4), approximately 54% of it’s mass will liberate the mass of 3 different alcohols. Contrast this to another agent that would generate ethanol by esterases, ethyl paraben (only 28% of it’s mass will liberate the mass of 1 alcohol, ethanol); it has a much lower mass efficiency to generate the EDIM. In addition, the larger size of these more mass efficient molecules will likely have a solid physical state, which simplifies integration into the MAMS pill system. Of course, the maximum EDIM concentration in the breath will be primarily dependent upon the mass of NCE, the intrinsic rate of generation of EDIM by enzyme(s), and the physiochemical characteristics of the EDIMs in the body. The isotopic labels shown in Table 2, preferably but not limited to deuterium, can be used to label various atoms of the NCE, which in turn, will generate a wide array of isotopically (approach described in Figures 29-34) and/or non-isotopically labeled alcohols that will serve as EDIMs in this example. In addition, Isotopic labeling of larger metabolic fragments derived from the parent (e.g., carboxylic acid in this embodiment), which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed. Note: the number of carbon linkages between the ring structure and the carbonyl bond can be varied to optimize the molecular properties of the molecule.

Ester Example 8: New Chemical Entity – Non-Cyclic Molecule Containing 3 Ester Bonds – Figure 36. Figure 36 illustrates an ester-based non-cyclic NCE that can generate 3 different alcohols (ethanol, n-propanol, and tert-butanol) as EDIMs. Each of the 3 ester bonds on the NCE will be hydrolyzed and release a carboxylic acid(s) and 3 different alcohols. At least 3 major advantages exist for creating these types of NCEs for MAMS applications: 1) it allows custom-designed patterns of EDIMs to be released via enzymes (either a single type or more than one type) that can provide excellent discrimination (e.g., combination of EDIMs in breath is highly distinctive and can be used to eliminate the effect
of diet or disease on MAMS function), 2) different combinatorial permutations (e.g., a single NCE containing one or more ester groups versus combinations of different NCEs, each containing one or more distinctive ester groups) of these types of molecules can be used to label different dosage forms of a given drug (e.g., warfarin) and/or multiple types of different medications, and 3) by combining distinctive EDIMs into a NCE, the mass of drug (preferred embodiment is the solid form) required to release these patterns of EDIMs can be minimized. The latter is important because mass limitations in a pill matrix for MAMS will exist. For example, for the NCE shown above (MW=344.4), approximately 52% of it’s mass will liberate the mass of 3 different alcohols. Contrast this to another agent that would generate ethanol by esterases, ethyl paraben (only 28% of it’s mass will liberate the mass of 1 alcohol, ethanol); it has a much lower mass efficiency to generate the EDIM. In addition, the larger size of these more mass efficient molecules will likely have a solid physical state, which simplifies integration into the MAMS pill system. Of course, the maximum EDIM concentration in the breath will be primarily dependent upon the mass of NCE, the intrinsic rate of generation of EDIM by enzyme(s), and the physiochemical characteristics of the EDIMs in the body. The isotopic labels shown in Table 2, preferably but not limited to deuterium, can be used to label various atoms of the NCE, which in turn, will generate a wide array of isotopically (approach described in Figures 29-34) and/or non-isotopically labeled alcohols that will serve as EDIMs in this example. In addition, Isotopic labeling of larger metabolic fragments derived from the parent (e.g., carboxylic acid in this embodiment), which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed. Note: the number of carbon linkages between the central carbon (indicated by asterisk) and the carbonyl bond can be varied to optimize the molecular properties of the molecule.

Ester Example 9: New Chemical Entity – Non-Cyclic Molecule Containing 4 Ester Bonds – Figure 37. Figure 37 illustrates an ester-based non-cyclic NCE that can generate 4 different alcohols (ethanol, n-propanol, tert-butanol, n-pentanol) as EDIMs. Each of the 4 ester bonds on the NCE will be hydrolyzed and release a carboxylic acid(s) and 4 different alcohols. At least 3 major advantages exist for creating these types of NCEs for MAMS applications: 1) it allows custom-designed patterns of EDIMs to be released via enzymes (either a single type or more than one type) that can provide excellent discrimination (e.g., combination of EDIMs in breath is highly distinctive and can be used to eliminate the effect
of diet or disease on MAMS function), 2) different combinatorial permutations (e.g., a single NCE containing one or more ester groups versus combinations of different NCEs, each containing one or more distinctive ester groups) of these types of molecules can be used to label different dosage forms of a given drug (e.g., warfarin) and/or multiple types of different medications, and 3) by combining distinctive EDIMs into a NCE, the mass of drug (preferred embodiment is the solid form) required to release these patterns of EDIMs can be minimized. The latter is important because mass limitations in a pill matrix for MAMS will exist. For example, for the NCE shown above (MW=500.67), approximately 52% of it’s mass will liberate the mass of 4 different alcohols. Contrast this to another agent that would generate ethanol by esterases, ethyl paraben (only 28% of it’s mass will liberate the mass of 1 alcohol, ethanol); it has a much lower mass efficiency to generate the EDIM. In addition, the larger size of these more mass efficient molecules will likely have a solid physical state, which simplifies integration into the MAMS pill system. Of course, the maximum EDIM concentration in the breath will be primarily dependent upon the mass of NCE, the intrinsic rate of generation of EDIM by enzyme(s), and the physiochemical characteristics of the EDIMs in the body. The isotopic labels shown in Table 2, preferably but not limited to deuterium, can be used to label various atoms of the NCE, which in turn, will generate a wide array of isotopically (approach described in Figures 29-34) and/or non-isotopically labeled alcohols that will serve as EDIMs in this example. In addition, Isotopic labeling of larger metabolic fragments derived from the parent (e.g., carboxylic acid in this embodiment), which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed. Note: the number of carbon linkages between the central carbon (indicated by asterisk) and the carbonyl bond can be varied to optimize the molecular properties of the molecule.

CYP450 Enzymes

Although many enzymatic systems biotransform drugs in humans, the most important and versatile one is the cytochrome P450 mixed function oxidase (MFO) system, especially for lipophilic xenobiotics. It is a remarkable system that has it roots of origin over 3.5 billion years ago. The CYP system is a heme containing, molecular oxygen requiring, membrane bound system containing over 160 known members. A reduced cofactor, NADPH+, and a coenzyme, cytochrome P450 NADPH oxidoeductase, are critical for P450 activity, whereas
a membrane bound hemoprotein, cytochrome b5, can further stimulate P450 catalytic activity, most notably for the 3A family. NADPH oxidoreductase transfers electrons from NADPH to the various isoforms of P450. The level of these factors can markedly affect the activity of the CYP components. P450 is primarily synthesized and located in the liver, but other production and location sites (e.g., small intestine, kidney) are known to exist. Hepatic P450 is located in the endoplasmic reticulum and mitochondria. It plays a major role in the metabolism of numerous physiological substrates such as prostaglandins, steroids, bile acids plus a large number of clinically important drugs. The CYP system is responsible for the reduction, oxidation and hydrolysis of lipophilic drugs. The two major CYP enzymes, CYP3A4 and CYP2D6 catalyze dealkylation, hydroxylation, dehalogenation, dehydration, and nitroreduction reactions. By incorporating various isotopic labels listed in Table 2 (preferred embodiment is deuterium) into the various atomic sites of the CYP450 substrates (e.g., including but not limited to deuterium for ordinary hydrogen; $^{17}$O and/or $^{18}$O for ordinary oxygen, or $^{13}$C for ordinary carbon, where appropriate), various EDIMs (arising from the CYP substrate, aldehyde, acid and CO$_2$) containing one or more isotopic labels could be generated that will fulfill the requirements of an effective MAMS. Shown below are ten examples of CYP450 substrates (Figures 38-47), which are FDA approved or GRAS-type drugs that could be isotopically labeled for an effective MAMS, and in some cases to create “smart” therapeutic agents:

CYP Substrate Example 1 - Enzyme: CYP-3A4 – Substrate: Verapamil – Figure 38. Verapamil (2,8-bis-(3,4-dimethoxyphenyl)-6-methyl-2-isopropyl-6-azaoctanitrile) is a L-type calcium channel blocker that liberates formaldehyde upon oxidative dealkylation (N-demethylation) by CYP-3A4. Orally administered verapamil undergoes extensive metabolism in the liver. One major metabolic pathway is the formation of norverapamil (N-methylated metabolite of verapamil) and formaldehyde by CYP-3A4. Although dependent upon the number of alternate metabolic pathways, the rate of formation of a specific metabolite(s) (i.e., verapamil $\rightarrow$ norverapamil and formaldehyde via CYP-3A4) generally appears to be predictive of in vivo functional enzyme competence. In fact verapamil is metabolized by O-demethylation (25%) and N-dealkylation (40%). The CYP-3A4 is most the important enzyme in humans for metabolizing drugs. It has been estimated that the CYP-3A4 isoform of the P450 system is responsible for metabolizing 55-60% of all pharmaceutical agents. The CYP3A4 plays a critical role in metabolizing many drugs,
including several cytotoxic drugs such as paclitaxel, docetaxel, vinorelbine, vincristine, irinotecan, topotecan, ifosfamide, cyclophosphamide, and tamoxifen. Thus, alterations in CYP-3A4 function frequently lead to drug-induced increases in morbidity and mortality. The isotopic labels shown in Table 2 (preferably deuterium), where appropriate, can be used to label various atoms (red circle) of verapamil, which in turn, will generate isotopic-labeled formaldehyde that will serve as the preferred embodiment of the EDIM in this example. In addition, isotopic labeling of larger metabolic fragments (e.g., norverapamil, etc.) derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

CYP Substrate Example 2 - Enzyme: CYP-3A4 – Substrate: Erythromycin – Figure 39. Erythromycin is a macrolide antibiotic, which prevents protein synthesis in bacteria, and is thus used to treat various infections, particularly in patients who are allergic to penicillin. Because erythromycin is also a potent motolol agonist, it markedly enhances gastric emptying. This gastrokinetic action is known to wane in a short period of time, due to the development of tachyphylaxis/desensitization. The erythromycin breath test (EBT) is used to assess CYP-3A4 function. Erythromycin is N-demethylated by CYP-3A4, and the cleaved methyl group is released as formaldehyde and, eventually, as formic acid then CO2. The test is performed by intravenously administering a trace amount of 14C labeled erythromycin and then measuring the amount of exhaled 14CO2. The rate of release of 14CO2 in expired breath is thought to reflect hepatic CYP3A4 activity. The isotopic labels shown in Table 2 (preferably deuterium), where appropriate, can be used to label various atoms (red circle) of erythromycin, which in turn, will generate isotopic-labeled formaldehyde that will serve as the preferred embodiment of the EDIM in this example. In addition, isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

CYP Substrate Example 3 - Enzyme: CYP-3A4 – Substrate: Amiodarone – Figure 40. Amiodarone is one of the most effective antiarrhythmic drugs in clinical medicine. It is highly effective in treating atrial fibrillation, particularly in preventing its re-occurrence. Although this drug has a complex mechanistic profile (blocks sodium channels, beta receptors, calcium channels, and potassium channels) its major electrophysiological action is to prolong repolarization in cardiac tissue, predominantly by blocking potassium channels.
Therefore, it is classified as a Class III antiarrhythmic drug according to the Vaughn-William Classification. The isotopic labels shown in Table 2 (preferably deuterium), where appropriate, can be used to label various atoms (red circle) of amiodarone, which in turn, will generate isotopic-labeled acetaldehyde that will serve as the preferred embodiment of the EDIM in this example. In addition, isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

CYP Substrate Example 4 - Enzyme: CYP-3A4 – Substrate: Propafenone – Figure 41. Propafenone is an antiarrhythmic drug that acts by primarily blocking sodium channels, and is classified as a Class IC antiarrhythmic drug according to the Vaughn-William Classification. The isotopic labels shown in Table 2 (preferably deuterium), where appropriate, can be used to label various atoms (red circle) of propafenone, which in turn, will generate isotopic-labeled propionaldehyde that will serve as the preferred embodiment of the EDIM in this example. In addition, isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

CYP Substrate Example 5 - Enzymes: CYP-3A4 + CYP-2D6 + Esterase – Substrate: Diltiazem – Figure 42. Diltiazem is a L-type calcium channel blocker, which undergoes complex biotransformation, including deacetylation, N-demethylation, and O-demethylation. Of these pathways, CYP-3A4 probably plays a more prominent role than CYP2D6 in the metabolism of diltiazem. The isotopic labels shown in Table 2 (preferably deuterium), where appropriate, can be used to label various atoms (red circle) of diltiazem, which in turn, will generate isotopic-labeled formaldehyde and/or acetic acid that will serve as the preferred embodiments of the EDIMs in this example. In addition, isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

CYP Substrate Example 6 - Enzyme: CYP-2D6 – Substrate: Flecainide – Figure 43. Flecainide is an antiarrhythmic drug that acts by primarily blocking sodium channels, and is classified as a Class IC antiarrhythmic drug according to the Vaughn-William Classification. Flecainide is characterized as a unique drug, given its high content of fluorine. CYP-2D6 liberates a highly distinctive, volatile fluorinated aldehyde metabolite, termed trifluoroaldehyde. The isotopic labels shown in Table 2 (preferably non-ordinary carbon),
where appropriate, can be used to label various atoms (red circle) of flecainide, which in turn, will generate isotopic-labeled trifluoroaldehyde that will serve as the preferred embodiment of the EDIM in this example. Note: the unique nature of fluorinated aldehyde will likely allow a MAMS to be constructed without the need for isotopic labeling in the case of flecainide. In addition, isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

CYP Substrate Example 7 - Enzyme: CYP-2D6 – Substrate: Codeine – Figure 44. Shown is an example where the CYP substrate is a prodrug (codeine) that is converted by the P450 system (CYP 2D6) into the active drug (morphine). Morphine has a significantly higher affinity for the μ opioid receptor than codeine, and thus is thought to mediate the analgesic properties of codeine. Only about 10% of codeine is normally converted to morphine in vivo. In this embodiment, the NICE system could be used to not only ensure that codeine is efficacious (i.e., ensures adequate conversion to morphine) but also to ensure that an inordinate amount of codeine isn’t converted to morphine if a subject has a super functional of CYP-2D6. The latter scenario would cause an adverse drug reaction (ADR) because an excessive amount of morphine would be present in the body. Likewise, in the former scenario, the NICE system would identify those subjects that wouldn’t get adequate pain relief from this drug, because not enough morphine is produced from codeine. The function of CYP 2D6 is altered by a great many factors including but not limited to genetics or drug-drug interactions. For example, because 6-10% of Caucasians have poorly functional CYP2D6, they do not get adequate pain relief from codeine. Furthermore, a number of medications are potent CYP2D6 inhibitors and reduce or even completely eliminate the efficacy of codeine. The most notorious of these are the SSRIs including fluoxetine (Prozac) and citalopram (Celexa). The high end PO dose of codeine is typically 240 mg given over 24 hours. The small arrow indicates the site of catalytic action by the CYP enzyme to liberate the formaldehyde. The isotopic labels shown in Table 2 (preferably deuterium), where appropriate, can be used to label various atoms (red circle) of codeine, which in turn, will generate isotopic-labeled formaldehyde that will serve as the preferred embodiment of the EDIM in this example. In addition, isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.
CYP Substrate Example 8 – Enzyme: CYP-1A2 – Substrate: Olanzapine – Figure 45. Olanzapine is one of the most widely used antipsychotic drugs in the world. It is used to treat schizophrenia. The major metabolic pathway for olanzapine is mediated by CYP-1A2. Its metabolism is well predicted by using the caffeine breath test as a probe to examine the ability of the CYP450 system to metabolism olanzapine. The small arrow indicates the site of catalytic action by the CYP enzyme to liberate the formaldehyde. The isotopic labels shown in Table 2 (preferably deuterium), where appropriate, can be used to label various atoms (red circle) of olanzapine, which in turn, will generate isotopic-labeled formaldehyde that will serve as the preferred embodiment of the EDIM in this example. In addition, isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

CYP Substrate Example 9 – Enzyme: CYP-1A2 – Substrate: Caffeine – Figure 46. Caffeine is a xanthine-type drug that is widely found in many foods, including beverages. Caffeine is a central nervous stimulant. It has been generally accepted as a specific in vivo probe for CYP1A2 activity. Approximately 80% of caffeine given orally to humans is converted to theophylline. Caffeine has been shown to provide an accurate phenotypic probe for measuring CYP1A2 activity, particularly when predicting the ability of olanzapine to be metabolized in vivo. The small arrow indicates the site of catalytic action by the CYP enzyme to liberate the formaldehyde. The isotopic labels shown in Table 2 (preferably deuterium), where appropriate, can be used to label various atoms (red circle) of caffeine, which in turn, will generate isotopic-labeled formaldehyde that will serve as the preferred embodiment of the EDIM in this example. In addition, isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

CYP Substrate Example 10 – Enzyme: CYP-2C – Substrate: Amphetamine – Figure 47. Amphetamine (alpha-methyl-phenethylamine) is a central nervous system (CNS) stimulant used primarily to treat attention-deficit hyperactivity disorder (ADHD) and narcolepsy. Unfortunately, the drug is widely used recreationally as a club drug and as a performance enhancer, and humans can be become highly addicted to this drug. The small arrow indicates the site of catalytic action by the CYP enzyme (CYP-2C) to liberate the ammonia via deamination. The isotopic labels shown in Table 2 (preferably non-ordinary
nitrogen and to a lesser degree deuterium), where appropriate, can be used to label various atoms (red circle) of amphetamine, which in turn, will generate isotopic-labeled ammonia that will serve as the preferred embodiment of the EDIM in this example. In addition, isotopic labeling of larger metabolic fragments derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

From the perspective of preventing ADRs and monitoring enzyme competency, there is one aspect of the CYP enzyme system that can be exploited. Most drugs are metabolized by oxidative N-dealkylation. It is commonly observed that the alkyl group lost from an amine during N-dealkylation (and from an ether during O-dealkylation) appears as an aldehyde or ketone arising from the dissociation of a carbinolamine intermediate. Aldehydes and ketones are volatile, so deuteration (or other form of isotopic labeling) of medications on the portion of the molecule that forms the aldehyde or ketone will result in a "reporter" that is volatile and will appear in the breath.

Deaminases – Adenosine Deaminase

Adenosine deaminase (also known as ADA) is an enzyme (EC 3.5.4.4) involved in purine metabolism. It very rapidly metabolizes the nucleoside adenosine ingested from food and/or produced from turnover of nucleic acids in tissues. Adenosine is an FDA approved drug for intravenous use in treating supraventricular tachyarrhythmias involving the AV node (via activation of A1 receptors that depress nodal conduction) and for improving the quality of cardiac perfusion scans (via A2 receptor-mediated dilation of coronary vessels). By removing an amine group, adenosine deaminase irreversibly deaminates adenosine to the related nucleoside, inosine. Inosine, in turn, can be deribosylated (removed from ribose) by another enzyme called purine nucleoside phosphorylase (PNP), converting it to hypoxanthine.

Figure 48 is illustrative of the above. Adenosine is a nucleoside, which is naturally found in the body, that is highly effective when given intravenously at treating reentrant supraventricular tachyarrhythmias involving the AV node as part of the reentrant circuit. By activating A1 receptors and increasing IKADO conductance, adenosine effectively terminates these rhythm disorders by profound depressing AV nodal conduction. Due to the rapid degradation by adenosine deaminase, which is ubiquitous in the body, orally administered
adenosine used for MAMS should effectively liberate ammonia without incurring a significant increase in plasma adenosine levels in the blood. The small arrow indicates the site of catalytic action by the CYP enzyme to liberate the ammonia. The isotopic labels shown in Table 2 (preferably non-ordinary nitrogen or deuterium), where appropriate, can be used to label various atoms (red circle) of adenosine, which in turn, will generate isotopic-labeled ammonia that will serve as the preferred embodiment of the EDIM in this example. In addition, isotopic labeling of larger metabolic fragments (e.g., inosine) derived from the parent, which could be semi-volatile or non-volatile, could also serve as EDIMs, particularly if the liquid phase of breath is being analyzed.

Implication in Drug Development of Using Isotopic Labeled Therapeutic Entities: A Summary of the Concept of “NICE” (New Intelligent Chemical Entity)

In this patent application, technologies are described that potentially create a new area in drug design research and development - the advent of “smart” or “intelligent” therapeutic agents. What is the definition of a “smart” drug? When humans use therapeutic agents to treat various medical disorders, two major limitations make these entities have suboptimal efficacy and safety: 1) non-adherence (patients don’t take the drugs as instructed by their health care provider in terms of dose and/or frequency), and/or 2) adverse drug reactions (ADRs) resulting from but not limited to drug-drug interactions (DDIs) or genetic defects (e.g., genetic polymorphisms in CYP enzymes including but not limited to 2D6, 2C9, 2C19; genetic polymorphism of vitamin K epoxide reductase [VKORC1] involving warfarin therapy). A “smart” therapeutic agent of the invention is designed to reliably and accurately “self report” key elements of its safety and efficacy during chronic therapy by incorporating 3 types of functions into a medication system:

1: continuously documenting a particular therapeutic agent was administered (preferable embodiment is ingestion of pill via oral route) at the right time intervals (frequency), hereafter termed \( F_{\text{Freq}} \)

2: continuously documenting a specific dose of a particular therapeutic agent was administered in the proper amount (dose), hereafter termed \( F_{\text{Dose}} \)

3: continuously documenting a particular therapeutic agent was being properly metabolized, hereafter termed \( F_{\text{Metab}} \)
By specifically engineering these functional attributes into a therapeutic agent, it would not only make pharmaceutical therapies safer and more efficacious, but also create new medications from either existing drugs (generic and/or on patent) with minimal-to-no new regulatory issues or create easy pathways to design and synthesize new molecular entities that have these beneficial functional attributes incorporated into the system from the inception of the molecule. These types of therapeutic agents, hereafter termed NICE (New "Intelligent" Chemical Entity)-type molecules, would represent a new paradigm in drug discovery and development. Unfortunately, thousands of drugs, both generic and patented, currently on the market being sold to consumers are not intelligent, but in fact are "dumb". That is, they provide no continuous feedback to patients and/or health care providers as to their efficacy and safety, which is particularly important when medications are given over sustained periods of time to treat a variety of diseases. With the current invention, generic or patented “dumb” drugs already on the market could be educated and made intelligent without incurring the liability of new regulatory hurdles, or alternately, new molecular entities being developed for different disease could be designed to be intelligent right from the start. The ideal NICE-type therapeutic agents would be trifunctional \( (F_{\text{Freq}}F_{\text{Dose}}F_{\text{Metab}}) \) in nature. In fact, having all 3 attributes would make them “genius” molecules. However, a number of different combinations of the 3 individual functions \( (F_{\text{Freq}}, F_{\text{Dose}}, \text{and/or } F_{\text{Metab}}) \) could be incorporated into a NICE system; therefore embodiments of the NICE system could be bifunctional or even monofunctional in nature. Figures 49 to 59 provides details and teaches how to construct these different types of “smart” medications systems, ranging from the most simple NICE-type medications (Figure 49) to among the most complex (Figure 55). In another embodiment, a fourth element called the therapeutic drug monitoring (TDM) function, termed the \( F_{\text{TDM}} \), could also be integrated into a medication system. For example, in one embodiment \( F_{\text{TDM}} \) could be integrated into \( F_{\text{Freq}}, F_{\text{Dose}}, \text{and } F_{\text{Metab}} \) to create a quad-functional “smart” pill system: \( F_{\text{Freq}}F_{\text{Dose}}F_{\text{Metab}}F_{\text{TDM}} \). \( F_{\text{TDM}} \) indicates the ability of a smart pill system to measure the concentration of the active therapeutic drug (A) in the blood, using a surrogate concentration of A in the breath, preferably using the liquid phase of breath. In this embodiment A may or may not be isotopically labeled (preferably with deuterium, see Table 2 for additional options).

In Figure 49A, a single taggant (Tcircles) is on pill surface containing the active therapeutic agent, A (which is not labeled). The \textbf{EDIM} is \textbf{Tcircles} (i.e., not a metabolite of...
T, T1circles). When placed in the mouth, a pill surface-derived EDIM (Tcircles) is immediately liberated and will activate a sensor (indicates detection of Tcircles), which is preferably portable and hand held, when a sample of exhaled breath is provided to the sensor. With this embodiment, immediate notification of pill ingestion and simplicity of system are provided.

In Figure 49B, two taggants (Tgray and Tblack) are on pill surface containing the active therapeutic agent, A. The EDIMs are Tgray and Tblack (i.e., not a metabolite of Tgray, T1gray; not a metabolite of Tblack, T1black). When placed in the mouth, two pill surface-derived EDIMs (Tgray and Tblack) are immediately liberated and will activate a sensor (indicates detection of Tgray and/or Tblack) when exhaled into. With this embodiment, immediate notification of pill ingestion and simplicity of system are provided. Further, chance of interference of EDIM detection by various factors (e.g., diet, metabolism, disease) is very low if Tgray and Tblack are simultaneously detected in breath. Note: In this figure different combinations of surface taggants (e.g., different pairs, different triads could be used to label different doses of a given drug or different drugs.

In Figure 49C, three taggants (Tdarkgray, Tlightgray, Tblack) are on pill surface containing the active therapeutic agent, A. The EDIMs are Tdarkgray, Tlightgray, Tblack (i.e., not a metabolite of Tdarkgray, T1darkgray; not a metabolite of Tlightgray, T1lightgray; not a metabolite of Tblack, T1black). When placed in the mouth, three pill surface-derived EDIMs (Tdarkgray, Tblack, Tlightgray) are immediately liberated and will activate a sensor (indicating detection of Tdarkgray, Tblack, and/or Tlightgray) when exhaled into. With this embodiment, immediate notification of pill ingestion and simplicity of system. Further, chance of interference of EDIM detection in breath by various factors (e.g., diet, metabolism, disease) is virtually impossible if Tdarkgray, Tlightgray, and Tblack are simultaneously detected in breath.

In Figure 50A, two taggants (Tgray and Tblack) are on pill surface containing the active therapeutic agent, A. The EDIMs are Tgray, Tblack, and a metabolite of Tgray, T1gray. When placed in the mouth, two pill surface-derived EDIMs (Tgray and Tblack) are immediately liberated and will activate a sensor when exhaled into shortly (detection of Tgray and Tblack) after ingesting the pill; later when Tgray enters the gastrointestinal tract (GIT) and is absorbed into the blood, it is metabolized to T1gray that will appear in the breath and activate the sensor when exhaled into (detection of T1gray). In this embodiment,
immediate notification of pill placement in mouth and confirmation of A entering the blood (pill entering GIT and being absorbed) is provided. One taggart (Tgray) provides dual functionality in this embodiment: 1) immediate confirmation of putting the pill in the mouth while 2) confirming the therapeutic drug actually entered the blood. Allows flexibility of confirming medication adherence on the basis of using either an early breath (Tgray and Tblack), a later breath (Tlightgray), or both. Literally guarantees ingestion of A. Very low chance of interference of EDIM detection by various factors (e.g., diet, metabolism, disease).

In Figure 50B, three taggants (Tdarkgray, Tlightgray, Tblack) are on pill surface containing the active therapeutic agent, A. The EDIMs are Tdarkgray, Tlightgray, Tblack and metabolite of Tblack, T1lightgray. Alternately, in this embodiment, it is not critical that Tblack be an EDIM, since the combination of Tdarkgray and Tlightgray will still provide excellent discrimination from breath interferants. When placed in the mouth, three pill surface-derived EDIMs (Tdarkgray, Tlightgray, Tblack) are immediately liberated and will activate a sensor (detection of Tdarkgray, Tlightgray, Tblack) when exhaled into after ingesting the pill; later when Tblack enters the GIT and is absorbed into the blood, it is metabolized to T1lightgray that will appear in the breath and activate the sensor when exhaled into (detection of T1lightgray). In this embodiment, the addition of the 3rd taggart (Tblack) provides extra EDIM discrimination that the pill was placed into the mouth. Interference of EDIM measurements by various factors (e.g., diet, metabolism, disease) is virtually impossible if Tdarkgray, Tlightgray, and Tblack are simultaneously detected in breath. Note: In this figure different combinations of surface taggants (e.g., different pairs, different triads could be used to label different doses of a given drug or different drugs.

In Figure 51A, two taggants (Tdarkgray and Tblack) located on the surface and one taggart (Tlightgray) is placed inside the pill in a manner that makes it physically distinct from the active therapeutic agent, A. The EDIMs are Tdarkgray, Tblack, and a metabolite of Tlightgray, T1lightgray. When placed in mouth, two pill surface-derived EDIMs (Tdarkgray and Tblack) are immediately liberated and will activate a sensor when exhaled into shortly (detection of Tdarkgray and Tblack) after ingesting the pill; later when Tlightgray enters the GIT and is absorbed into the blood, it is metabolized to T1lightgray that will appear in the breath and activate the sensor when exhaled into (detection of T1lightgray). This embodiment is similar to that of Figure 50B, wherein this embodiment provides immediate notification of pill placement in mouth and confirmation of A entering the blood.
(pill entering the GIT and being absorbed). One taggant (Tlightgray) serves only to indicate that the pill contents entered the blood. Its placement inside the pill (versus on the surface—as illustrated in Figure 50B) makes Tlightgray a more efficient source of T1lightgray (more reliable delivery to GIT and blood entry), and hence improves the quality of MAMS. Note: In this figure different combinations of surface taggants (e.g., different pairs analogous to Tdarkgray and Tblack) could be used to label different doses of a drug or different drugs.

In Figure 51B, two taggants (Tdarkgray, Tblack, ) are on the pill surface and two taggants (Tlightgray1, Tlightgray2) are within the pill containing the active therapeutic agent, A. The EDIMs are Tdarkgray, Tblack, metabolite of Tlightgray1, T1lightgray1 and metabolite of Tlightgray2, T1lightgray2. This embodiment is nearly identical to that of Figure 51A except one additional taggant (Tlightgray2) was added that generates a second metabolite-based EDIM (T1lightgray2) in addition to T1lightgray1 that confirms the pill contents entered the GIT and subsequently the blood. Thus, in this embodiment, the MAMS system has 2 taggants that confirm placement of the pill into the mouth, and 2 taggants that will confirm the subject actually took the pill. By adding two taggants for each function, the reliability of the system will become much greater than if one was used for each. In addition, placing Tlightgray1 and Tlightgray2 inside the pill will increase the reliability of the system in terms of making the generation of their respective metabolites more reliable and efficient.

In Figure 52, two taggants (Tgray and Tblack) are both placed on the surface of an isotopic-labeled therapeutic agent, *A. Note: In previous embodiments (Figures 49-51), A was not labeled with non-ordinary isotopes. The EDIMs are Tgray, Tblack, and metabolite of *A, *A1. When placed in the mouth, two pill surface-derived EDIMs (Tgray and Tblack) are immediately liberated and will activate a sensor when exhaled into shortly (detection of Tgray and Tblack). Later, after ingesting the pill, *A enters the GIT, absorbed in the blood, and then metabolized to *A1, which will appear in the breath and activate the breath sensor (detection of *A1). Different surface taggants could be used to label different doses of *A. This embodiment provides immediate notification of pill ingestion and confirmation of pill ingestion. The chance of interference of EDIM detection to document the pill was placed in the mouth by various factors (e.g., diet, metabolism, disease) is very low if Tgray and Tblack are simultaneously detected in breath. *A provides confirmation that the pill was actually ingested. In addition, if a medication can become “self reporting” in terms of their metabolism, it would markedly improve drug safety.
In Figure 53, two taggants (Tgray and Tblack) are both placed on the surface of an isotopic-labeled therapeutic agent, *A. Note; in previous embodiments (Figures 49-51), A was not labeled with non-ordinary isotopes. The EDIM are Tgray, Tblack, and metabolite of *A, *A1. The only difference between this embodiment and that of Figure 52 is the mass of isotopic-labeled active therapeutic drug in the pill. In the example shown, only 0.1% of the mass of the active therapeutic drug located within the capsule contains non-ordinary isotopes. Given the signal-to-noise ratio that isotopic labeled EDIM (derived from *A) provides, there is no reason to label the majority of the mass of A. The preferred amount of *A in the pill is the least amount of *A that stills provides an adequate *A-based EDIM signal and thus an effective MAMS.

In Figure 54, two taggants (Tdarkgray and Tblack) located on the surface and one taggant (Tlightgray) is placed inside the pill in a manner that makes it physically distinct from the isotope-labeled active therapeutic agent, *A. The EDIMs are Tdarkgray, Tblack, and a metabolite of Tlightgray, T1lightgray, and a metabolite of *A, *A1. When placed in mouth, two pill surface-derived EDIMs (Tdarkgray and Tblack) are immediately liberated and will activate a sensor when exhaled into shortly (detection of Tdarkgray and Tblack) after ingesting the pill; later, when Tlightgray enters the GIT and is absorbed into the blood, it is metabolized to T1lightgray that will appear in the breath and activate the sensor when exhaled into (detection of T1lightgray). The only difference between this embodiment and that of Figure 52 is the addition of a taggant, Tlightgray, inside the pill. Likewise, Tlightgray could be placed on the pill surface, preferably in a more protected manner than Tdarkgray and Tblack. Since using *A1 alone is problematic for assessing drug adherence (see Figure 52), Tlightgray will address this issue. In fact, in this embodiment, Tlightgray serves not only to indicate that the pill contents entered the blood (definitive adherence) but also provides a critical comparator required to properly assess the metabolism of *A to *A1. The latter relates to correcting for changes in gastric emptying and/or drug absorption. Its placement inside the pill (versus on the surface) makes Tlightgray a more efficient source of T1lightgray (more reliable delivery to the GIT and blood entry), and hence improves the quality of MAMS. The active therapeutic drug will “self report” its metabolism via *A1 EDIM breath concentrations and adjustments will be made using Tlightgray.

In Figure 55, two taggants (Tdarkgray, Tblack) on the pill surface and two taggants (Tlightgray1, Tlightgray) within the pill containing the active therapeutic agent, A. In this
embodiment, A does not contain a non-ordinary isotope. The EDIMs are Tdarkgray, Tblack, a metabolite of Tlightgray1, T1lightgray1, and a metabolite of Tlightgray2, T1lightgray2. When placed in mouth, two pill surface-derived EDIMs (Tdarkgray and Tblack) are immediately liberated and will activate a sensor when exhaled into shortly (detection of Tdarkgray and Tblack) after ingesting the pill; later when Tlightgray1 and Tlightgray2 enter the GIT and are absorbed into the blood, it is metabolized to T1lightgray1 and T1lightgray2 that will appear in the breath and activate the sensor when exhaled into (detection of T1lightgray1 and T1lightgray2). The only difference between this embodiment and that of Figure 54 is the addition of a tagant, Tlightgray2, inside the pill, alongside Tlightgray1. In this embodiment, like that of Figure 54, Tlightgray is metabolized by a different enzyme than that for A, preferably a high capacity, rapidly acting blood-based enzyme (e.g., butyrylcholinesterase). In contrast, Tlightgray2 is metabolized by the same major enzyme, termed E, as that of A. In other words, Tlightgray2 (via conversion by E to T1lightgray2) will be used as a probe to continuously assess the metabolism of A to A1. In some cases, excellent probes exist that can predict the metabolism of key therapeutic agents. This approach has many advantages: 1) no requirement to isotopically label A, 2) not limited by mass or half life of A in terms of detecting breath A1 to assess metabolism of A, and 3) probes exist that accurately predict metabolism of important drugs. To illustrate this concept, the desmethylation of the antipsychotic olanzapine (Figure 45) by CYP-1A2 to liberate formaldehyde is well predicted by caffeine (Figure 46) when used as an enzyme probe. Olanzapine is potent (typical dose = 10 mg PO QD). Given its long half life and low dose, olanzapine won’t generate high breath A1 concentrations. In contrast, a much greater mass (typical dose is hundreds of mg per day orally) of the GRAS-food additive caffeine can be safely given to humans, which will markedly increase the signal-to-noise ratio (e.g., levels of deuterated breath formaldehyde) and accurately predict the metabolism of olanzapine. TGreen functions independent of TGray and is still required to ensure the pill was actually ingested (see Figure 52 for discussion) and to provide adequate corrections for GIT factors. Figure 56 illustrates how this system would work.

Figures 56A-C show the weekly EDIM concentration-time relations in a subject after swallowing a pill (having the architecture of MAMS-11) once per day over 3 weeks. Panel A, B and C illustrate the EDIM concentration-time relations at Day 7, Day 14, and Day 21, respectively, of therapy with active therapeutic drug A. To measure the EDIM
concentrations, end tidal (alveolar values) is the phase of breath preferred, particularly for the more volatile EDIMs. At Day 7, Day 14, and Day 21, the subject regularly and reliably placed the pill in his/her mouth (i.e., CMax of Tdarkgray and CMax of Tblack were unchanged over the 3 weeks). Likewise, because CMax of Tlightgray1 did not vary between weeks, it appears this subject has minimal variation in his/her gastric emptying/absorption of the pill. During the first two weeks of therapy, the metabolism of Tlightgray2 (taggart substrate that is metabolized by the same enzyme that metabolizes A to A1) is stable. However, at Day 21 the CMax ratio of Tlightgray2:Tlightgray1 plummeted by 5-fold (0.96 to 0.19), indicating the metabolism of Tlightgray2 was likely to be severely reduced. Because this ratio takes into account Tlightgray1, this reduction in Tlightgray2 cannot be attributed to alterations in GIT function (gastric emptying, absorption). It was later learned the subject was placed on a 5th medication that caused a DDI (inhibited the CYP450 enzyme that metabolized both Tlightgray2 and A). Note: Other parameters that could be used in the analysis include but are not limited to area under the concentration-time curve (AUC), rate of increase and/or decrease of EDIM concentrations, and time to maximum concentration (TMax). In embodiments such as this embodiment where FMetab is assessed, the preferred measure of EDIMs used to assess drug metabolism is quantitative; assessment of surface EDIM markers to indicate placement of the pill in the mouth can be semi-quantitative or even qualitative.

In Figure 56D, two taggants (Tdarkgray, Tblack) on the pill surface and two taggants (Tlightgray1, Tlightgray2) within the pill containing the active therapeutic agent, A. In this embodiment, A does not contain a non-ordinary isotope. The EDIMs are Tdarkgray, Tblack, a metabolite of Tlightgray1, Tlightgray1, and a metabolite of Tlightgray2, Tlightgray2. When placed in mouth, two pill surface-derived EDIMs (Tdarkgray and Tblack) are immediately liberated and will activate a sensor when exhaled into shortly (detection of Tdarkgray and Tblack) after ingesting the pill; later when Tlightgray1 and Tlightgray2 enter the GIT and are absorbed into the blood, it is metabolized to Tlightgray1 and Tlightgray2 that will appear in the breath and activate the sensor when exhaled into (detection of Tlightgray1 and Tlightgray2). Please see Figure 55 for a description of the function of Tlightgray1 and Tlightgray2.

In Figures 57A-C, three sets of dual taggants located on the pill surface containing the active therapeutic agent, A are used to label three different doses of A. The three sets of
surface taggants include a) Tdarkgray -Tblack (low dose A), b) Tlightgray -Tdarkergray2 (intermediate dose A), and c) Tlightgray2 -Tdarkergray3 (high dose A). The surface taggants could be solid-based and/or liquids contained in biodegradable capsules adhered to the surface of A. The EDIMs are Tdarkgray -Tblack (low dose A); Tlightgray -Tdarkergray2 (intermediate dose A); Tlightgray2 -Tdarkergray3 (high dose A). When placed in the mouth, two pill surface-derived EDIMs for each dose form are immediately liberated and will activate a sensor (indicates detection of the two taggants for each dose) when exhaled into.

In this embodiment, immediate notification of pill ingestion and simplicity of system are provided. Further, chance of interference of EDIM detection by various factors (e.g., diet, metabolism, disease) is very low using dual system of surface taggants, particularly when they are simultaneously detected in breath.

In Figures 58A-C, three different dose forms of a given active therapeutic agent, A, are surfaced labeled by using different markers, consisting but not limited to a total of seven taggants (Twhite, Tdarkgray, Tblack, Tlightgray, Tdarkgray2, Tlightgray2, Tdarkgray2) on the pill surface containing the active therapeutic agent, A. In this embodiment, one taggart (Twhite) is used to label the active therapeutic agent, which has multiple dose forms. The other six taggants are used to label the dose; in this embodiment, two unique surface taggants are used to label the dose form: 1) low dose: Tdarkgray and Tblack; 2) intermediate dose: Tlightgray and Tdarkgray2; and 3) high dose: Tlightgray2 and Tdarkgray3. The surface taggants could be solid-based and/or liquids contained in biodegradable capsules adhered to the surface of A. The EDIMs are 1) low dose: Twhite, Tdarkgray and Tblack; 2) intermediate dose: Twhite, Tlightgray and Tdarkgray2; and 3) high dose: Twhite, Tlightgray2 and Tdarkgray3. When a given dose of active therapeutic agent A is placed in the mouth, three pill surface-derived EDIMs are immediately liberated and will activate a sensor when exhaled into, indicating placement of drug A and a specific dose of drug A into the mouth. In this embodiment, immediate notification of pill ingestion and simplicity of system is provided. Further, chance of interference of EDIM detection in breath by various factors (e.g., diet, metabolism, disease) is very low with multiple surface taggant system, particularly if they are simultaneously detected in breath.

In Figures 59A-C, three different dose forms of a given active therapeutic agent, A, are surfaced labeled by using different surface markers, consisting of seven taggants (Twhite, Tdarkgray, Tblack, Tlightgray, Tdarkgray2, Tlightgray2, Tdarkgray2) “loosely” attached and
one taggent (Tdarkoutline) firmly adherent to the pill surface containing the active therapeutic agent, A. One taggent (Twhite) is used to label the active therapeutic agent, which has multiple dose forms. Another taggent (Tdarkoutline), via enzymatic (preferably a blood-based enzyme) generation of a metabolite, T1darkoutline, is used to guarantee the pill contents entered the blood of the subject following GIT absorption. The remaining six taggants are used to label the dose. In this embodiment, two unique surface taggants are used to label the dose form: 1) low dose: Tdarkgray and Tblack; 2) intermediate dose: Tlightgray and Tdarkgray2; and 3) high dose: Tlightgray2 and Tdarkgray3. In this embodiment, 7 surface taggants (Twhite, Tdarkgray, Tblack, Tlightgray, Tdarkgray2, Tlightgray2, Tdarkgray3) are designed to be easily released in the mouth, whereas the one surface tightly adherent taggent (Tdarkoutline) is designed to be preferentially released in the stomach or more distal GIT locations (e.g., duodenum). These taggants could be solid-based and/or liquids contained in biodegradable capsules attached, either loosely and/or tightly, to the surface of A. The EDIMs are T1darkoutline plus 1) low dose: Twhite, Tdarkgray and Tblack; 2) intermediate dose: Twhite, Tlightgray and Tdarkgray2; and 3) high dose: Twhite, Tlightgray2 and Tdarkgray3. When a given dose of active therapeutic agent A is placed in the mouth, three pill surface-derived EDIMs are immediately liberated and will activate a sensor when exhaled into, indicating placement of drug A and a specific dose of drug A into the mouth. This embodiment is the same as that of Figure 58 except a taggent Tdarkoutline has been added that generates T1darkoutline, which confirms the pill contents entered the blood and the pill was actually ingested. In the preferred embodiment, Tdarkoutline is firmly attached to the surface of the active therapeutic agent (i.e., does not dislodge or be released in the mouth) or integrated into the gel matrix of a hard gel capsule and therefore neither alters the matrix of A nor the require a separate compartment within the pill (which still keeps Tdarkoutline apart from the matrix of A).

Below is a succinct description of the components and features of various NICE systems and the rationale behind them.

**Sensors:** To create NICE-type therapeutic agents, the measurement of various entities, either from the active drug and/or associated taggants *per se* or from their respective metabolites, will be measured using sensing technology, preferred but not limited to being portable point-of-use devices. The types of sensors were previously disclosed in the above
patents (Section A), but include and are not limited to the various types of infrared spectroscopy (gas or liquid based) with or without GC or mGC, mass spectroscopy (SIFT, GC, liquid), infrared, Raman, GC-MS, and neutron diffraction. The sensors would use various biological media including breath, blood, urine etc. In a preferred embodiment a sensor could use two types of sensing technologies (e.g., IR and mGC-CMOS), which would in turn provide a much greater level of discrimination between molecular entities (drugs and taggants) if stable isotope labeling was combined with discrimination of say alcohols.

**Key Characteristics of NICE:** Multiple types of NICE-type therapeutic agents are created by assembling different combinations of different types of design elements into the system (Figures 49-59). These elements provide a chemical framework whereby the system can optimally (reliably, reproducibly, and accurately) assess $F_{	ext{Feq}}$, $F_{	ext{Dose}}$, and/or $F_{	ext{Metab}}$, and correct for factors that would confound interpretation and function of the NICE system. These factors include: 1) correction for variable gastric emptying (e.g., slowing of gastrophysiology due to stress, consumption of fatty meals, or drugs) and/or absorption that can alter oral drug pharmacokinetics such as area under the concentration-time curve (AUC), time to maximal concentration ($T_{\text{max}}$) and maximal concentration ($C_{\text{max}}$), 2) detection and correction for impaired enzyme function (e.g., secondary to genetic polymorphisms, drug-drug interactions (DDIs), pathophysiological disturbances) that may mask administration (false negative) of drug ingestion when it was actually imbibed, if the exhaled drug ingestion marker(s) (EDIM) is generated via that particular enzyme, 3) provide a high degree of discrimination of detecting volatile (or semi-volatile, and even non-volatile) markers in the breath against a background of endogenous production of similar or identical substance or dietary intake of substances in foods/drinks (e.g. effects of fatty meals on bioavailability, generation of volatile markers used in the NICE system), and 4) generate markers, termed exhaled drug ingestion markers (EDIMs) in the breath, which are suitable for NICE systems (e.g., duration neither too short nor too long; reliably appears in the breath). Indeed, the comparator, as described in Option 2 of Section B3, not only would ensure that the metabolism of the active therapeutic drug A was being metabolized normally, but also could be used as an index of gastric emptying in a variety of clinical settings.

Features of these NICE elements include but are not limited to the following:

- the active therapeutic drug could be a generic drug, patented drug, or other type of pharmacutic.
• the taggant(s) could be associated with A by surface coating, physically locating them in
different compartments of a capsule/pill, or integrating the taggant into the excipient
matrix of a pill or capsule. The preferred embodiment is to place the taggant in a manner
that does not alter the FDA-approved pill matrix (e.g., taggant integrated into the matrix
of a hard gel capsule that contains the API inside it).

5 • A taggant should be added to correct for changes in gastroesophageal emptying,
absorption, metabolic incompetence of specific enzymes.

• The dose of an active pharmaceutical drug could be determined using the NICE system
by associating different doses of the active therapeutic agent with the following strategies:
10 a) incorporate different isotopes on various parts of the active therapeutic agent’s and/or
taggants’ molecular structures in the NICE system, preferably on those that liberate
volatile (or semi-volatile) metabolic fragments upon enzyme degradation; this dose not
exclude non-ordinary isotopic labeling of larger, non-volatile fragments of the parent
compound; b) incorporate variable extents of a given isotopic label (e.g., deuterium) on
the active therapeutic agent and/or taggants in the NICE system, c) incorporate
combinations of a and b in the NICE system, and/or d) incorporate different doses of a
given taggant with or without isotopic labeling place.

• The taggants could be any Class 1, 2 and/or 3 drugs (see Section A) including but not
limited to new chemical entities or GRAS-type compounds, which may or may not be
labeled with non-ordinary isotopes (see Table 2).

• The isotopic labels could be located on one or more locations of active drug(s) or
taggant(s). The active therapeutic agent and associated taggant(s), and their respective
metabolites may or may not utilize isotopic labels in the NICE system.

• A molecule, either the active therapeutic agent (A) and/or taggant (T), could contain a
single or different types of stable isotopic labels (see Table 2).

• The enzymes used to degrade the compound(s) to generate various EDIMs may or may
not be the same as the primary enzyme used to degrade the active therapeutic agent, A.
The enzymes involved in the NICE system could include but are not limited to: a)
oxidative metabolism involving CYP450, including but not limited to important isoforms
for drug metabolism such as CYP-3A4 and CYP-2D6, or those impacted by genetic
polymorphisms (CYP-2D6, 2C19, 2C9), b) VKORC1 in the setting of warfarin therapy,
c) esterases including but not limited to pseudocholinesterase, carboxylesterases, PON1,
and acetylcholinesterase, etc.), d) dehydrogenases (alcohol and aldehyde), and e) enzymes not listed above but listed in the patent (Table 1).

- The enzyme substrates used in the NICE system, which entail the active therapeutic agent, drug salt (S), excipients (E) and/or taggants (if present), when acted upon by CYP450, esterases, and/or other enzymes, will generate volatile (or semivolatile, nonvolatile) markers that appear in the breath, termed the EDIMs. These breath markers, which themselves can be Class 1, 2 and/or 3 drugs or be derived by metabolism of Class 1, 2 and/or 3 drugs, will include but are not limited to alcohols, aldehydes, ketones, and acids. Section B.2 lists all relevant chemicals. Alternately, in some embodiments of the invention, the active therapeutic agent and/or the taggant(s) itself may be detected in the breath.

- The enzyme substrates (active therapeutic agents and/or taggants) of the NICE system could be in physical state of solid, liquid or gas. Solid or liquids having lower volatility are the preferred embodiments in the NICE system for the active therapeutic drug and taggants.

- A subject may blow (preferentially once but be more than once in a given session) into the device to rapidly check for $F_{\text{Freq}}F_{\text{Dose}}F_{\text{Metab}}$, or at a less frequent basis (e.g., once per week or month) blow repeatedly into the device at fixed time intervals over a longer period of time (e.g., 1-3 hrs) to get a complete breath concentration-time relationship to fully assess metabolic competence.

- The sensor of the NICE system may or may not be linked to a biometric (e.g., fingerprint, retinal scan)

Another means to produce drugs for the above applications, which would be both economically feasible and straightforward in terms of detection, includes modifying (labeling) known compounds (Class I through III type agents, see above) with a stable isotope (see Table 1 for examples using in biology) including, but not limited to, deuterium (heavy water, or heavy hydrogen). In preferred embodiment, the isotopic label would stable (non-radioactive), and be deuterium. Deuterium is a stable, non-radioactive isotope of hydrogen that is found naturally, which contains 1 proton and 1 neutron electron. The number of protons plus neutrons is called the atomic mass number. An isotope is an atom with the same number of electrons and protons, but with a different number of neutrons. In other words, atoms with the same atomic number but different atomic weights are called
isotopes. Because specific types of isotopes have an identical number of electrons, they belong to the same element and behave almost the same in chemical reactions. Therefore, in medicine isotopes such as deuterium have been used to label biologically important molecules in metabolic studies as a non-radioactive isotopic tracer because chemically it behaves very similarly to hydrogen, is essentially non-toxic, and can be readily distinguished from hydrogen using infrared (IR) or mass spectrometry. Although other non-radioactive stable isotopes (see Table 1) such as carbon (e.g., $^{13}$C) could be used in these technologies, deuterium is strongly preferred because it can be more readily detected and discriminated from endogenous molecules containing ordinary hydrogen using inexpensive, portable, point-of-care and point-of-use sensing technologies such as IR. Either a deuterated parent molecule containing the deuterium label and/or a key volatile (or semi-volatile) metabolite(s) of the parent molecule (generated via enzyme metabolism) containing the deuterium would be detected in the breath.

Deuterium, depending upon the class of molecules they are placed on, the number of deuterations on a molecule, and their proximity to various bond types (e.g., amine, sulphydryl, aromatic, etc.) on the molecule, can provide various types of molecular entities with unique analytical “signatures” in various biological media, including but not limited to breath, blood, urine, sweat or saliva. Various analytical techniques such as IR or mass spectroscopy can be used to not only distinguish deuterated parent compounds from their deuterated metabolites (both in the gas and/or liquid states), but can also easily discriminate deuterated molecules from those identical natural compounds containing ordinary hydrogen (e.g., ethanol versus deuterated alcohol; aldehyde versus deuterated aldehyde; methanol versus deuterated methanol). The use of deuterium can be applied to all of the inventions listed above. Its use will reduce the need or even eliminate the step of obtaining baseline breath samples, as well as markedly simplify (or even eliminate) the FDA regulatory process for new drugs allowing for faster time to market with inexpensive and reliable technology.

Deuterated compounds are generally regarded as nontoxic and of having the same (or very similar) pharmacodynamic (PD) and pharmacokinetic (PK; ADME) properties as their undeuterated parent compounds. Further, deuteration can be applied to several new related inventions (which can also be practiced with the more conventional Class 1 through 3 agents disclosed for medical diagnostic applications). They are:
• "New Intelligent Chemical Entity" (NICE)-type therapeutic agents for medication adherence monitoring. Three different types of NICE-type agents exist for medication adherence in this application: 1) the parent therapeutic agent being used to treat a medical disorder is labeled with deuterium and upon metabolism (e.g., via enzymatic action) will generate a volatile (or semi-volatile) marker in the breath containing the deuterium label, 2) the therapeutic agent is not labeled per se with deuterium but upon metabolism (e.g., via enzymatic action) will generate a volatile or semi-volatile (not deuterated) marker that can be detected in the breath, and 3) the therapeutic agent is neither labeled with deuterium nor generates a measurable volatile (or semi-volatile) marker in the breath, but is rather associated with a taggant (that may be either labeled or unlabeled with deuterium), which in turn will generate a marker in the breath that is easily measurable. The taggant can be part of the excipient matrix/salt of the therapeutic drug, can be coated onto the surface of the therapeutic drug, or be physically separate from the therapeutic drug. The preferred taggant embodiment is the latter case where the excipient matrix of the active therapeutic drug is not altered by the presence of the taggant.

• NICE-type drugs to assess enzyme competency. Three different types of NICE compounds exist for assessing enzyme competency in this application: 1) the parent therapeutic agent would contain a deuterated label and would itself "report" whether the individual taking the medication is competent for the enzyme required to metabolize itself by measuring a deuterated metabolite of the parent drug in the breath, and 2) the parent therapeutic agent would not contain a deuterated label but would still itself "report" whether the individual taking the medication is competent for the enzyme required to metabolize itself by measuring a metabolite (non-deuterated) of the parent drug in the breath, and 3) the taggant, either labeled or not labeled with non-ordinary isotopes, associated with the active therapeutic agent A would "report" whether the individual taking the drug is competent for the enzyme required to metabolize A. NICE-type agents used for enzyme competency could have additional taggant(s) added, besides the ones mentioned above, which would serve a number of important roles: a) an enzyme calibrator by being a substrate for the same or different enzyme as the one degrading the therapeutic agent, and b) an index of
gastric emptying to correct for the effect of varied gastric clearance on enzyme competency results.

- The means to synthesize taggants or modified pharmaceutics is disclosed in detail in the prior patent applications, as are lists of GRAS and other compounds which can be used to monitor adherence, enzyme competency and drug diversion. As previously disclosed, most medications are metabolized by the P450 enzyme system, with the CYP2D6 and CYP3A4 isoforms accounting for about 83% of drug metabolism (3A4 - 50% and 2D6 - 33%). With so many drugs metabolized by a limited number of enzymes, there is often competition for metabolism. Likewise, genetics can alter the function of many of these CYP enzymes (e.g., CYP 2D6, CYP 2C9, CYP 2C19). Also, certain drugs can induce P450 enzymes and actually reduce blood concentrations of other drugs. With the average individual over 65 years of age taking 4 or more medications, it is not surprising that there are frequent adverse drug reactions (ADRs). It is estimated that over 700,000 serious reactions and deaths result from DDIs.

- Although these drugs can be potentially given via various routes (oral, intravenous, sublingual, rectal, intramuscular, inhalation, subcutaneous, intrasynovial, intracardiac, intrathecal, intratracheal, buccal, eye, nasal, ear, rectum, vaginal, urethral, transdermal/topical), the preferred administration routes will be oral and sublingual.

- Combining adherence monitoring and enzyme competency reporting in a NICE-type therapeutic agent is novel, particularly when it is done in a continuous basis and is an intrinsic part of the therapeutic agent (EDIM is generated from the therapeutic agent or from a taggant physically associated with the therapeutic agent).

- The dual function of a NICE-type therapeutic agent could come from one specific area of the parent molecule or from more than one area of the molecule. For example, a specific metabolic fragment of a NICE would indicate adherence, where another fragment of a NICE would indicate it is being metabolized properly or improperly. In another embodiment, a specific fragment of a NICE would indicate both adherence and metabolic functions.

- If a therapeutic agent undergoes metabolism by multiple enzymes, multiple taggants (either labeled or not labeled with stable isotopes), could be added to monitor its metabolism. For example, let's say a chemical entity termed X undergoes P450
oxidation metabolism via CYP-3A4 and CYP-2D6. Two taggants, termed T_{3A4} and T_{2D6}, either labeled with or without an isotope (e.g., deuterium), which are known substrates for CYP-3A4 and CYP-2D6, respectively, would be physically associated with X. Volatile (or semi-volatile) fragments from T_{3A4} and T_{2D6} that appear in body fluids such as the breath, could be used to quantitate metabolism via the different pathways of X.

- To document MAM, if a taggant approach is used, then the taggant may be metabolized by a different enzyme system than the therapeutic agent. This may be advantageous since alterations in the enzyme that degrades the active therapeutic agent A may diminish the ability to use it as a MAMs marker, if it is not being metabolized property. To get around this limitation and to eliminate changes in esophageal/gastric motility with oral pill ingestion, a comparator taggant could be added, which will document that the components of the pill are being delivered to the blood and liver, and we can normalize the AUC and/or C_{Max} to document things (Figures 54-56).

- The isotope label could be incorporated into the active therapeutic agent in two ways: 1) 100% of the active therapeutic agent contains the isotopic label (Figure 52), or 2) only a fraction of the active therapeutic agent (Figure 53).

In this patent application, technologies are described that catalyze a new strategy in drug design and drug research and development - “smart” (self monitoring and reporting therapeutics) drugs. By markedly reducing the incidence of ADRs and ensuring medication adherence, NICE-type agents will markedly improve both drug safety and efficacy while simultaneously reducing health care costs. Unique features about NICE-type drugs are that the “reporter” (EDIM) is a stable isotopic label entity (e.g., deuterium) as well the disclosure of new medical uses for exhaled breath. Stable isotopes present several advantages over all of the previously disclosed taggants and detection devices. First, a stable isotope such as deuterium should be regarded by the FDA to be safe and having minimal-to-no effect on PK/PD. Isotope (e.g., deuterated)-labeled chemicals are readily available, mostly for calibration of analytical equipment used for therapeutic drug monitoring and synthesis of deuterated analogues is straightforward and inexpensive. Further, deuteration of a compound
changes the IR spectrum (liquid and gas phases) so that the deuterated analog can be easily distinguished from the parent compound.

The technology outlined in this invention will not only allow monitoring of medication adherence and enzymatic (metabolic) competence on a continuous on-going basis to make therapies (acute and chronic) drugs more safe and efficacious, but can be readily adapted to address other areas of national and international importance including drug counterfeiting, drug diversion and therapeutic drug monitoring (TDM) using cost effective technologies.

It should be understood that the scope of the claims should not be limited by the preferred embodiments set forth in the examples, but should be given the broadest interpretation consistent with the description as a whole.
APPENDIX A
Table 1: Relevant Enzymes to the Design of New Intelligent Chemical Entity (NICE)-type Therapeutic Agents: Adapted from the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (NC-IUBMB)

EC 1. Oxidoreductases

EC 1.1 Acting on the CH-OH group of donors

**EC 1.1.1** With NAD$^+$ or NADP$^+$ as acceptor

- **EC 1.1.1.1** alcohol dehydrogenase
- **EC 1.1.1.2** alcohol dehydrogenase (NADP$^+$)
- **EC 1.1.1.3** homoserine dehydrogenase
- **EC 1.1.1.4** (R,R)-butanediol dehydrogenase
- **EC 1.1.1.5** acetoin dehydrogenase
- **EC 1.1.1.6** glycerol dehydrogenase
- **EC 1.1.1.7** propanediol-phosphate dehydrogenase
- **EC 1.1.1.8** glycerol-3-phosphate dehydrogenase (NAD$^+$)
- **EC 1.1.1.9** D-xylulose reductase
- **EC 1.1.1.10** L-xylulose reductase
- **EC 1.1.1.11** D-arabinitol 4-dehydrogenase
- **EC 1.1.1.12** L-arabinitol 4-dehydrogenase
- **EC 1.1.1.13** L-arabinitol 2-dehydrogenase
- **EC 1.1.1.14** L-iditol 2-dehydrogenase
- **EC 1.1.1.15** D-iditol 2-dehydrogenase
- **EC 1.1.1.16** galactitol 2-dehydrogenase
- **EC 1.1.1.17** mannitol-1-phosphate 3-dehydrogenase
- **EC 1.1.1.18** inositol 2-dehydrogenase
- **EC 1.1.1.19** glucuronate reductase
- **EC 1.1.1.20** glucuronolactone reductase
- **EC 1.1.1.21** aldehyde reductase
- **EC 1.1.1.22** UDP-glucose 6-dehydrogenase
- **EC 1.1.1.23** histidinol dehydrogenase
- **EC 1.1.1.24** quinate dehydrogenase
- **EC 1.1.1.25** shikimate dehydrogenase
- **EC 1.1.1.26** glyoxy late reductase
- **EC 1.1.1.27** L-lactate dehydrogenase
- **EC 1.1.1.28** D-lactate dehydrogenase
- **EC 1.1.1.29** glycerate dehydrogenase
- **EC 1.1.1.30** 3-hydroxybutyrate dehydrogenase
- **EC 1.1.1.31** 3-hydroxyisobutyrate dehydrogenase (NAD$^+$)
- **EC 1.1.1.32** mevalonate reductase
- **EC 1.1.1.33** mevalonate reductase (NADPH)
- **EC 1.1.1.34** hydroxymethylglutaryl-CoA reductase (NADPH)
- **EC 1.1.1.35** 3-hydroxyacyl-CoA dehydrogenase
- **EC 1.1.1.36** acetoacetyl-CoA reductase
- **EC 1.1.1.37** malate dehydrogenase
- **EC 1.1.1.38** malate dehydrogenase (oxaloacetate-decarboxylating)
- **EC 1.1.1.39** malate dehydrogenase (decarboxylating)
- **EC 1.1.1.40** malate dehydrogenase (oxaloacetate-decarboxylating) (NAD$^+$)
- **EC 1.1.1.41** isocitrate dehydrogenase (NAD$^+$)
- **EC 1.1.1.42** isocitrate dehydrogenase (NADP$^+$)
- **EC 1.1.1.43** phosphogluconate 2-dehydrogenase
- **EC 1.1.1.44** phosphogluconate dehydrogenase (decarboxylating)
EC 1.1.1.45 L-gulonate 3-dehydrogenase
EC 1.1.1.46 L-arabinose 1-dehydrogenase
EC 1.1.1.47 glucose 1-dehydrogenase
EC 1.1.1.48 galactose 1-dehydrogenase
EC 1.1.1.49 glucose-6-phosphate dehydrogenase
EC 1.1.1.50 3α-hydroxysteroid dehydrogenase (B-specific)
EC 1.1.1.51 3(or 17)β-hydroxysteroid dehydrogenase
EC 1.1.1.52 3α-hydroxycholestanate dehydrogenase
EC 1.1.1.53 3α(or 20β)-hydroxysteroid dehydrogenase
EC 1.1.1.54 allyl-alcohol dehydrogenase
EC 1.1.1.55 lactaldehyde reductase (NADPH)
EC 1.1.1.56 ribitol 2-dehydrogenase
EC 1.1.1.57 fructuronate reductase
EC 1.1.1.58 tagaturonate reductase
EC 1.1.1.59 3-hydroxypropionate dehydrogenase
EC 1.1.1.60 2-hydroxy-3-oxopropionate reductase
EC 1.1.1.61 4-hydroxybutyrate dehydrogenase
EC 1.1.1.62 estradiol 17β-dehydrogenase
EC 1.1.1.63 testosterone 17β-dehydrogenase
EC 1.1.1.64 testosterone 17β-dehydrogenase (NADP⁺)
EC 1.1.1.65 pyridoxine 4-dehydrogenase
EC 1.1.1.66 α-hydroxydecanoate dehydrogenase
EC 1.1.1.67 mannitol 2-dehydrogenase
EC 1.1.1.68 now EC 1.7.99.5
EC 1.1.1.69 gluconate 5-dehydrogenase
EC 1.1.1.70 deleted, included in EC 1.2.1.3
EC 1.1.1.71 alcohol dehydrogenase [NAD(P)⁺]
EC 1.1.1.72 glycerol dehydrogenase (NADP⁺)
EC 1.1.1.73 octanol dehydrogenase
EC 1.1.1.74 deleted
EC 1.1.1.75 (R)-aminopropanal dehydrogenase
EC 1.1.1.76 (S,S)-butanediol dehydrogenase
EC 1.1.1.77 lactaldehyde reductase
EC 1.1.1.78 methylglyoxal reductase (NADH-dependent)
EC 1.1.1.79 glyoxylate reductase (NADP⁺)
EC 1.1.1.80 isopropanol dehydrogenase (NADP⁺)
EC 1.1.1.81 hydroxypropyruvate reductase
EC 1.1.1.82 malate dehydrogenase (NADP⁺)
EC 1.1.1.83 D-malate dehydrogenase (decarboxylating)
EC 1.1.1.84 dimethylmalate dehydrogenase
EC 1.1.1.85 3-isopropylmalate dehydrogenase
EC 1.1.1.86 ketol-acid reductoisomerase
EC 1.1.1.87 homoisocitrate dehydrogenase
EC 1.1.1.88 hydroxymethylglutaryl-CoA reductase
EC 1.1.1.89 deleted, included in EC 1.1.1.86
EC 1.1.1.90 aryl-alcohol dehydrogenase
EC 1.1.1.91 aryl-alcohol dehydrogenase (NADP⁺)
EC 1.1.1.92 oxalosuccinate reductase (decarboxylating)
EC 1.1.1.93 tartrate dehydrogenase
EC 1.1.1.94 glycerol-3-phosphate dehydrogenase [NAD(P)⁺]
EC 1.1.1.95 phosphoglycerate dehydrogenase
EC 1.1.1.96 diiodophenylpyruvate reductase
EC 1.1.1.97 3-hydroxybenzyl-alcohol dehydrogenase
EC 1.1.1.98 (R)-2-hydroxy-fatty-acid dehydrogenase
EC 1.1.1.99 (S)-2-hydroxy-fatty-acid dehydrogenase
EC 1.1.1.100 3-oxoacyl-[acyl-carrier-protein] reductase
EC 1.1.1.101 acylglycerone-phosphate reductase
EC 1.1.1.102 3-dehydroshinganine reductase
EC 1.1.1.103 L-threonine 3-dehydrogenase
EC 1.1.1.104 4-oxoproline reductase
EC 1.1.1.105 retinol dehydrogenase
EC 1.1.1.106 pantotet 4-dehydrogenase
EC 1.1.1.107 pyridoxal 4-dehydrogenase
EC 1.1.1.108 carnitine 3-dehydrogenase
EC 1.1.1.109 now EC 1.3.1.28
EC 1.1.1.110 indolelactate dehydrogenase
EC 1.1.1.111 3-(imidazol-5-yl)lactate dehydrogenase
EC 1.1.1.112 indanol dehydrogenase
EC 1.1.1.113 L-xylene 1-dehydrogenase
EC 1.1.1.114 apiose 1-reductase
EC 1.1.1.115 ribose 1-dehydrogenase (NADP⁺)
EC 1.1.1.116 D-arabinose 1-dehydrogenase
EC 1.1.1.117 D-arabinose 1-dehydrogenase [NAD(P)⁺]
EC 1.1.1.118 glucose 1-dehydrogenase (NAD⁺)
EC 1.1.1.119 glucose 1-dehydrogenase (NADP⁺)
EC 1.1.1.120 galactose 1-dehydrogenase (NADP⁺)
EC 1.1.1.121 aldose 1-dehydrogenase
EC 1.1.1.122 D-threo-aldose 1-dehydrogenase
EC 1.1.1.123 sorbose 5-dehydrogenase (NAD⁺)
EC 1.1.1.124 fructose 5-dehydrogenase (NAD⁺)
EC 1.1.1.125 2-deoxy-D-gluconate 3-dehydrogenase
EC 1.1.1.126 2-dehydro-3-deoxy-D-gluconate 6-dehydrogenase
EC 1.1.1.127 2-dehydro-3-deoxy-D-gluconate 5-dehydrogenase
EC 1.1.1.128 L-idonate 2-dehydrogenase
EC 1.1.1.129 L-threonate 3-dehydrogenase
EC 1.1.1.130 3-dehydro-L-gulonate 2-dehydrogenase
EC 1.1.1.131 mannuronate reductase
EC 1.1.1.132 GDP-mannose 6-dehydrogenase
EC 1.1.1.133 dTDP-4-dehydroorhamnose reductase
EC 1.1.1.134 dTDP-6-deoxy-L-talose 4-dehydrogenase
EC 1.1.1.135 GDP-6-deoxy-D-talose 4-dehydrogenase
EC 1.1.1.136 UDP-N-acetylgulosamine 6-dehydrogenase
EC 1.1.1.137 ribitol-5-phosphate 2-dehydrogenase
EC 1.1.1.138 mannitol 2-dehydrogenase (NADP⁺)
EC 1.1.1.139 deleted, included in EC 1.1.1.21
EC 1.1.1.140 sorbitol-6-phosphate 2-dehydrogenase
EC 1.1.1.141 15-hydroxyprostaglandin dehydrogenase (NAD⁺)
EC 1.1.1.142 D-pinitol dehydrogenase
EC 1.1.1.143 sequoyitol dehydrogenase
EC 1.1.1.144 perillyl-alcohol dehydrogenase
EC 1.1.1.145 3β-hydroxy-85-steroid dehydrogenase
EC 1.1.1.146 11β-hydroxysteroid dehydrogenase
EC 1.1.1.147 16α-hydroxysteroid dehydrogenase
EC 1.1.1.148 estradiol 17α-dehydrogenase
EC 1.1.1.149 20α-hydroxysteroid dehydrogenase
EC 1.1.1.150 21-hydroxyesteroid dehydrogenase (NAD⁺)
EC 1.1.1.151 21-hydroxyesteroid dehydrogenase (NADP⁺)
EC 1.1.1.152 3α-hydroxy-5β-androstan-17-one 3α-dehydrogenase
EC 1.1.1.153 sepiapterin reductase
EC 1.1.1.154 ureidoglycolate dehydrogenase
EC 1.1.1.155 identical to EC 1.1.1.87
EC 1.1.1.156 glycerol 2-dehydrogenase (NADP⁺)
EC 1.1.1.157 3-hydroxybutyryl-CoA dehydrogenase
EC 1.1.1.158 UDP-N-acetylglucosamine dehydrogenase
EC 1.1.1.159 7α-hydroxysteroid dehydrogenase
EC 1.1.1.160 dehydrobunolol dehydrogenase
EC 1.1.1.161 cholestanetetraol 26-dehydrogenase
EC 1.1.1.162 erythulose reductase
EC 1.1.1.163 cyclopentanol dehydrogenase
EC 1.1.1.164 hexadecanol dehydrogenase
EC 1.1.1.165 2-alkyn-1-ol dehydrogenase
EC 1.1.1.166 hydroxycyclohexane-1-carboxylate dehydrogenase
EC 1.1.1.167 hydroxymalonate dehydrogenase
EC 1.1.1.168 2-dehydropantolactone reductase (A-specific)
EC 1.1.1.169 2-dehydropantoate 2-reductase
EC 1.1.1.170 3β-hydroxy-4α-methylcholestene-3-carboxylate 3-dehydrogenase
(decarboxylating)
EC 1.1.1.171 now EC 1.5.1.20
EC 1.1.1.172 2-oxoadipate reductase
EC 1.1.1.173 L-rhamnose 1-dehydrogenase
EC 1.1.1.174 cyclohexane-1,2-diol dehydrogenase
EC 1.1.1.175 D-xylose 1-dehydrogenase
EC 1.1.1.176 12α-hydroxysteroid dehydrogenase
EC 1.1.1.177 glycerol-3-phosphate 1-dehydrogenase (NADP⁺)
EC 1.1.1.178 3-hydroxy-2-methylbutyryl-CoA dehydrogenase
EC 1.1.1.179 D-xylose 1-dehydrogenase (NADP⁺)
EC 1.1.1.180 deleted, included in EC 1.1.1.131
EC 1.1.1.181 cholest-5-ene-3β,7α-diol 3β-dehydrogenase
EC 1.1.1.182 deleted, included in EC 1.1.1.198, EC 1.1.1.227 and EC 1.1.1.228
EC 1.1.1.183 geraniol dehydrogenase
EC 1.1.1.184 carbonyl reductase (NADPH)
EC 1.1.1.185 L-glycol dehydrogenase
EC 1.1.1.186 dTDP-galactose 6-dehydrogenase
EC 1.1.1.187 GDP-4-dehydro-d-rhamnose reductase
EC 1.1.1.188 prostaglandin-F synthase
EC 1.1.1.189 prostaglandin-E₄ 9-reductase
EC 1.1.1.190 indole-3-acetaldehyde reductase (NADH)
EC 1.1.1.191 indole-3-acetaldehyde reductase (NADPH)
EC 1.1.1.192 long-chain-alcohol dehydrogenase
EC 1.1.1.193 5-amino-6-(5-phosphoribosylamino)uracil reductase
EC 1.1.1.194 coniferyl-alcohol dehydrogenase
EC 1.1.1.195 cinnamyl-alcohol dehydrogenase
EC 1.1.1.196 15-hydroxyprostaglandin-D dehydrogenase (NADP⁺)
EC 1.1.1.197 15-hydroxyprostaglandin dehydrogenase (NADP⁺)
EC 1.1.1.198 (+)-borneol dehydrogenase
EC 1.1.1.199 (S)-usnate reductase
EC 1.1.1.200 aldose-6-phosphate reductase (NADPH)
EC 1.1.1.201 7β-hydroxycholesterol dehydrogenase (NADP⁺)
EC 1.1.1.202 1,3-propanediol dehydrogenase
EC 1.1.1.203 uronate dehydrogenase
EC 1.1.1.204 now EC 1.17.1.4
EC 1.1.1.205 IMP dehydrogenase
EC 1.1.1.206 tropine dehydrogenase
EC 1.1.1.207 (-)-menthol dehydrogenase
EC 1.1.1.208 (+)-neomenthol dehydrogenase
EC 1.1.1.209 3(or 17)-α-hydroxysteroid dehydrogenase
EC 1.1.1.210 3β(or 20α)-hydroxysteroid dehydrogenase
EC 1.1.1.211 long-chain-3-hydroxyacyl-CoA dehydrogenase
EC 1.1.1.212 3-oxoacyl-[acyl-carrier-protein] reductase (NADH)
EC 1.1.1.213 3α-hydroxysteroid dehydrogenase (A-specific)
EC 1.1.1.214 2-dehydropantolactone reductase (B-specific)
EC 1.1.1.215 gluconate 2-dehydrogenase
EC 1.1.1.216 farnesol dehydrogenase
EC 1.1.1.217 benzyl-2-methyl-hydroxybutyrate dehydrogenase
EC 1.1.1.218 morphine 6-dehydrogenase
EC 1.1.1.219 dihydrokaempferol 4-reductase
EC 1.1.1.220 6-pyruvoyl tetrahydropterin 2'-reductase
EC 1.1.1.221 vomifoliol 4'-dehydrogenase
EC 1.1.1.222 (R)-4-hydroxyphenyllactate dehydrogenase
EC 1.1.1.223 isopiperitenol dehydrogenase
EC 1.1.1.224 mannose-6-phosphate 6-reductase
EC 1.1.1.225 chlordecone reductase
EC 1.1.1.226 4-hydroxycyclohexanecarboxylate dehydrogenase
EC 1.1.1.227 (-)-borneol dehydrogenase
EC 1.1.1.228 (+)-sabinol dehydrogenase
EC 1.1.1.229 diethyl 2-methyl-3-oxosuccinate reductase
EC 1.1.1.230 3α-hydroxyglycyrhretinate dehydrogenase
EC 1.1.1.231 15-hydroxyprostaglandin-I dehydrogenase (NADP')
EC 1.1.1.232 15-hydroxyicosatetraenoate dehydrogenase
EC 1.1.1.233 N-acetylmannosamine 1-dehydrogenase
EC 1.1.1.234 flavanone 4-reductase
EC 1.1.1.235 8-oxoconoformycin reductase
EC 1.1.1.236 tropinone reductase
EC 1.1.1.237 hydroxyphenylpyruvate reductase
EC 1.1.1.238 12β-hydroxysteroid dehydrogenase
EC 1.1.1.239 3α(17β)-hydroxysteroid dehydrogenase (NAD')
EC 1.1.1.240 N-acetylhexosamine 1-dehydrogenase
EC 1.1.1.241 6-endo-hydroxycineole dehydrogenase
EC 1.1.1.242 now EC 1.3.1.69 zeatin reductase
EC 1.1.1.243 carveol dehydrogenase
EC 1.1.1.244 methanol dehydrogenase
EC 1.1.1.245 cyclohexanol dehydrogenase
EC 1.1.1.246 pterocarpin synthase
EC 1.1.1.247 codeinone reductase (NADPH)
EC 1.1.1.248 salutaridine reductase (NADPH)
EC 1.1.1.249 reinstated as EC 2.5.1.46
EC 1.1.1.250 D-arabinitol 2-dehydrogenase
EC 1.1.1.251 galactitol-1-phosphate 5-dehydrogenase
EC 1.1.1.252 tetrahydroxynaphthalene reductase
EC 1.1.1.253 now EC 1.5.1.33
EC 1.1.1.254 (S)-carnitine 3-dehydrogenase
EC 1.1.1.255 mannitol dehydrogenase
EC 1.1.1.256 fluoren-9-ol dehydrogenase
EC 1.1.1.257 4-(hydroxymethyl)benzenesulfonate dehydrogenase
EC 1.1.1.258 6-hydroxyhexanoate dehydrogenase
EC 1.1.1.259 3-hydroxyipimelolyl-CoA dehydrogenase
EC 1.1.1.260 sulcatone reductase
EC 1.1.1.261 glycerol-1-phosphate dehydrogenase [NAD(P)']
EC 1.1.1.262 4-hydroxythreonine-4-phosphate dehydrogenase
EC 1.1.1.263 1,5-anhydro-D-fructose reductase
EC 1.1.1.264 L-idonate 5-dehydrogenase
EC 1.1.1.265 3-methylbutanal reductase
EC 1.1.1.266 dTDP-4-dehydro-6-deoxyglucose reductase
EC 1.1.1.267 1-deoxy-D-xylulose-5-phosphate reductoisomerase
EC 1.1.1.268 2-(R)-hydroxypropyl-CoM dehydrogenase
EC 1.1.1.269 2-(S)-hydroxypropyl-CoM dehydrogenase
EC 1.1.1.270 3-keto-steroid reductase
EC 1.1.1.271 GDP-L-fucose synthase
EC 1.1.1.272 (R)-2-hydroxypropionic dehydrogenase
EC 1.1.1.273 vellosimine dehydrogenase
EC 1.1.1.274 2,5-didehydroxygluconate reductase
EC 1.1.1.275 (+)-trans-carveol dehydrogenase
EC 1.1.1.276 serine 3-dehydrogenase
EC 1.1.1.277 3β-hydroxy-5β-steroid dehydrogenase
EC 1.1.1.278 3β-hydroxy-5α-steroid dehydrogenase
EC 1.1.1.279 (R)-3-hydroxyacid ester dehydrogenase
EC 1.1.1.280 (S)-3-hydroxyacid ester dehydrogenase
EC 1.1.1.281 GDP-4-dehydro-6-deoxy-D-mannose reductase
EC 1.1.1.282 quinate/shikimate dehydrogenase
EC 1.1.1.283 methylglyoxal reductase (NADPH-dependent)
EC 1.1.1.284 S-(hydroxymethyl)glutathione dehydrogenase
EC 1.1.1.285 3′′-deamin-3′′-oxonicotianamine reductase
EC 1.1.1.286 isocitrate—homoisocitrate dehydrogenase
EC 1.1.1.287 D-arabinitol dehydrogenase (NADP+)
EC 1.1.1.288 xanthoxin dehydrogenase
EC 1.1.1.289 sorbose reductase
EC 1.1.1.290 4-phosphoerythronate dehydrogenase

**EC 1.1.2 With a cytochrome as acceptor**
EC 1.1.2.1 now EC 1.1.99.5
EC 1.1.2.2 mannitol dehydrogenase (cytochrome)
EC 1.1.2.3 L-lactate dehydrogenase (cytochrome)
EC 1.1.2.4 D-lactate dehydrogenase (cytochrome)
EC 1.1.2.5 D-lactate dehydrogenase (cytochrome c-553)

**EC 1.1.3 With oxygen as acceptor**
EC 1.1.3.1 deleted, included in EC 1.1.3.15
EC 1.1.3.2 now EC 1.1.3.12.4
EC 1.1.3.3 malate oxidase
EC 1.1.3.4 glucose oxidase
EC 1.1.3.5 hexose oxidase
EC 1.1.3.6 cholesterol oxidase
EC 1.1.3.7 aryl-alcohol oxidase
EC 1.1.3.8 L-gulonolactone oxidase
EC 1.1.3.9 galactose oxidase
EC 1.1.3.10 pyranose oxidase
EC 1.1.3.11 L-sorbose oxidase
EC 1.1.3.12 pyridoxine 4-oxidase
EC 1.1.3.13 alcohol oxidase
EC 1.1.3.14 catechol oxidase (dimerizing)
EC 1.1.3.15 (S)-2-hydroxy-acid oxidase
EC 1.1.3.16 ecdysone oxidase
EC 1.1.3.17 choline oxidase
EC 1.1.3.18 secondary-alcohol oxidase
EC 1.1.3.19 4-hydroxymandelate oxidase
EC 1.1.3.20 long-chain-alcohol oxidase
EC 1.1.3.21 glycerol-3-phosphate oxidase
EC 1.1.3.22 now EC 1.17.3.2
EC 1.1.3.23 thiamin oxidase
EC 1.1.3.24 L-galactonolactone oxidase
EC 1.1.3.25 now included with EC 1.1.99.18
EC 1.1.3.26 now EC 1.21.3.2
EC 1.1.3.27 hydroxyphytanate oxidase
EC 1.1.3.28 nucleoside oxidase
EC 1.1.3.29 N-acylhexosamine oxidase
EC 1.1.3.30 polyvinyl-alcohol oxidase
EC 1.1.3.31 deleted
EC 1.1.3.32 now EC 1.14.21.1
EC 1.1.3.33 now EC 1.14.21.2
EC 1.1.3.34 now EC 1.14.21.3
EC 1.1.3.35 now EC 1.14.21.4
EC 1.1.3.36 now EC 1.14.21.5
EC 1.1.3.37 D-arabinono-1,4-lactone oxidase
EC 1.1.3.38 vanillyl-alcohol oxidase
EC 1.1.3.39 nucleoside oxidase (H2O2-forming)
EC 1.1.3.40 D-mannitol oxidase
EC 1.1.3.41 xylitol oxidase

**EC 1.1.4 With a disulfide as acceptor**
- EC 1.1.4.1 vitamin-K-epoxide reductase (warfarin-sensitive)
- EC 1.1.4.2 vitamin-K-epoxide reductase (warfarin-insensitive)

**EC 1.1.5 With a quinone or similar compound as acceptor**
- EC 1.1.5.1 deleted, see EC 1.1.99.18
- EC 1.1.5.2 quinoprotein glucose dehydrogenase

**EC 1.1.99 With other acceptors**
- EC 1.1.99.1 choline dehydrogenase
- EC 1.1.99.2 2-hydroxyglutarate dehydrogenase
- EC 1.1.99.3 gluconate 2-dehydrogenase (acceptor)
- EC 1.1.99.4 dehydrogluconate dehydrogenase
- EC 1.1.99.5 glycerol-3-phosphate dehydrogenase
- EC 1.1.99.6 D-2-hydroxy-acid dehydrogenase
- EC 1.1.99.7 lactate — malate transhydrogenase
- EC 1.1.99.8 alcohol dehydrogenase (acceptor)
- EC 1.1.99.9 pyridoxine 5-dehydrogenase
- EC 1.1.99.10 glucose dehydrogenase (acceptor)
- EC 1.1.99.11 fructose 5-dehydrogenase
- EC 1.1.99.12 sorbose dehydrogenase
- EC 1.1.99.13 glucoside 3-dehydrogenase
- EC 1.1.99.14 glycolate dehydrogenase
- EC 1.1.99.15 now EC 1.7.99.5
- EC 1.1.99.16 malate dehydrogenase (acceptor)
- EC 1.1.99.17 now EC 1.1.5.2
- EC 1.1.99.18 cellubiose dehydrogenase (acceptor)
- EC 1.1.99.19 deleted
- EC 1.1.99.20 alkan-1-ol dehydrogenase (acceptor)
- EC 1.1.99.21 D-sorbitol dehydrogenase (acceptor)
- EC 1.1.99.22 glycerol dehydrogenase (acceptor)
- EC 1.1.99.23 polyvinyl-alcohol dehydrogenase (acceptor)
EC 1.1.99.24 hydroxoyacid-o xoacid transhydrogenase
EC 1.1.99.25 quinate dehydrogenase (pyrroloquinoline-quinone)
EC 1.1.99.26 3-hydroxyycloclohexanone dehydrogenase
EC 1.1.99.27 (R)-pantolactone dehydrogenase (flavin)
EC 1.1.99.28 glucose-fructose oxidoreductase EC 1.1.99.29 pyranose dehydrogenase (acceptor)
EC 1.1.99.30 2-oxoacid reductase

EC 1.2 Acting on the aldehyde or oxo group of donors

EC 1.2.1 With NAD\(^+\) or NADP\(^+\) as acceptor

EC 1.2.1.1 deleted, replaced by EC 1.1.1.284 and EC 4.4.1.22
EC 1.2.1.2 formate dehydrogenase
EC 1.2.1.3 aldehyde dehydrogenase (NAD\(^+\))
EC 1.2.1.4 aldehyde dehydrogenase (NADP\(^+\))
EC 1.2.1.5 aldehyde dehydrogenase [NAD(P)\(^+\)]
EC 1.2.1.6 deleted
EC 1.2.1.7 benzaldehyde dehydrogenase (NADP\(^+\))
EC 1.2.1.8 betaine-aldehyde dehydrogenase
EC 1.2.1.9 glyceraldehyde-3-phosphate dehydrogenase (NADP\(^+\))
EC 1.2.1.10 acetaldehyde dehydrogenase (acylating)
EC 1.2.1.11 aspartate-semialdehyde dehydrogenase
EC 1.2.1.12 glyceraldehyde-3-phosphate dehydrogenase (phosphorylating)
EC 1.2.1.13 glyceraldehyde-3-phosphate dehydrogenase (NAD\(^+\)) (phosphorylating)
EC 1.2.1.14 now EC 1.1.1.205
EC 1.2.1.15 malonate-semialdehyde dehydrogenase
EC 1.2.1.16 succinate-semialdehyde dehydrogenase [NAD(P)\(^+\)]
EC 1.2.1.17 glyoxylic acid dehydrogenase (acylating)
EC 1.2.1.18 malonate-semialdehyde dehydrogenase (acylating)
EC 1.2.1.19 aminobutyraldehyde dehydrogenase
EC 1.2.1.20 glutarate-semialdehyde dehydrogenase
EC 1.2.1.21 glycolaldehyde dehydrogenase
EC 1.2.1.22 lactaldehyde dehydrogenase
EC 1.2.1.23 2-oxoaldehyde dehydrogenase (NAD\(^+\))
EC 1.2.1.24 succinate-semialdehyde dehydrogenase
EC 1.2.1.25 2-oxoisovalerate dehydrogenase (acylating)
EC 1.2.1.26 2,5-dioxovalerate dehydrogenase
EC 1.2.1.27 methylmalonate-semialdehyde dehydrogenase (acylating)
EC 1.2.1.28 benzaldehyde dehydrogenase (NAD\(^+\))
EC 1.2.1.29 aryl-aldehyde dehydrogenase
EC 1.2.1.30 aryloxy-aldehyde dehydrogenase (NADP\(^+\))
EC 1.2.1.31 L-aminoacidipate-semialdehyde dehydrogenase
EC 1.2.1.32 aminomuconate-semialdehyde dehydrogenase
EC 1.2.1.33 (R)-dehydrodipentolate dehydrogenase
EC 1.2.1.34 deleted, included in EC 1.1.1.131
EC 1.2.1.35 now EC 1.1.1.203
EC 1.2.1.36 retinal dehydrogenase
EC 1.2.1.37 now EC 1.1.1.204
EC 1.2.1.38 N-acetyl-\(\gamma\)-glutamyl-phosphate reductase
EC 1.2.1.39 phenylacetaldehyde dehydrogenase
EC 1.2.1.40 3a,7a,12a-trihydroxycholestan-26-al 26-oxidoreductase
EC 1.2.1.41 glutamate-5-semialdehyde dehydrogenase
EC 1.2.1.42 hexadecanal dehydrogenase (acylating)
EC 1.2.1.43 formate dehydrogenase (NADP\(^+\))
EC 1.2.1.44 cinnamoyl-CoA reductase
EC 1.2.1.45 4-carboxy-2-hydroxymuconate-6-semialdehyde dehydrogenase
EC 1.2.1.46 formaldehyde dehydrogenase
EC 1.2.1.47 4-trimethylammoniobutyraldehyde dehydrogenase
EC 1.2.1.48 long-chain-aldehyde dehydrogenase
EC 1.2.1.49 2-oxoaldehyde dehydrogenase (NADP⁺)
EC 1.2.1.50 long-chain-fatty-acyl-CoA reductase
EC 1.2.1.51 pyruvate dehydrogenase (NADP⁺)
EC 1.2.1.52 oxoglutarate dehydrogenase (NADP⁺)
EC 1.2.1.53 4-hydroxyphenylacetaldehyde dehydrogenase
EC 1.2.1.54 γ-guanidinobutyraldehyde dehydrogenase
EC 1.2.1.55 now EC 1.1.1.279
EC 1.2.1.56 now EC 1.1.1.280
EC 1.2.1.57 butanal dehydrogenase
EC 1.2.1.58 phenylglyoxylate dehydrogenase (acylating)
EC 1.2.1.59 glyceraldehyde-3-phosphate dehydrogenase (NAD(P)⁺) (phosphorylating)
EC 1.2.1.60 5-carboxymethyl-2-hydroxymuconic-semialdehyde dehydrogenase
EC 1.2.1.61 4-hydroxymuconic semialdehyde dehydrogenase
EC 1.2.1.62 4-formylbenzenesulphonate dehydrogenase
EC 1.2.1.63 6-oxohexanoate dehydrogenase
EC 1.2.1.64 4-hydroxybenzaldehyde dehydrogenase
EC 1.2.1.65 salicylaldehyde dehydrogenase
EC 1.2.1.66 mycothiol-dependent formaldehyde dehydrogenase
EC 1.2.1.67 vanillin dehydrogenase
EC 1.2.1.68 coniferyl-aldehyde dehydrogenase
EC 1.2.1.69 fluoroacetalddehyde dehydrogenase
EC 1.2.1.70 glutamyl-tRNA reductase
EC 1.2.1.71 succinylglutamate-semialdehyde dehydrogenase
EC 1.2.1.72 erythrosc-4-phosphate dehydrogenase

EC 1.2.2 With a cytochrome as acceptor
  EC 1.2.2.1 formate dehydrogenase (cytochrome)
  EC 1.2.2.2 pyruvate dehydrogenase (cytochrome)
  EC 1.2.2.3 formate dehydrogenase (cytochrome-c-553)
  EC 1.2.2.4 carbon-monoxide dehydrogenase (cytochrome-b-561)

EC 1.2.3 With oxygen as acceptor
  EC 1.2.3.1 aldehyde oxidase
  EC 1.2.3.2 now EC 1.1.3.22
  EC 1.2.3.3 pyruvate oxidase
  EC 1.2.3.4 oxalate oxidase
  EC 1.2.3.5 glyoxylate oxidase
  EC 1.2.3.6 pyruvate oxidase (CoA-acetylating)
  EC 1.2.3.7 indole-3-acetaldehyde oxidase
  EC 1.2.3.8 pyridoxal oxidase
  EC 1.2.3.9 aryl-aldehyde oxidase
  EC 1.2.3.10 deleted
  EC 1.2.3.11 retinal oxidase
  EC 1.2.3.12 now EC 1.14.13.82
  EC 1.2.3.13 4-hydroxyphenylpyruvate oxidase
  EC 1.2.3.14 abscisic aldehyde oxidase

EC 1.2.4 With a disulfide as acceptor
  EC 1.2.4.1 pyruvate dehydrogenase (acetyl-transferring)
  EC 1.2.4.2 oxoglutarate dehydrogenase (succinyl-transferring)
  EC 1.2.4.3 deleted, included in EC 1.2.4.4
EC 1.2.4.4 3-methyl-2-oxobutanoate dehydrogenase (2-methylpropanoyl-transferring)

**EC 1.2.7 With an iron-sulfur protein as acceptor**

EC 1.2.7.1 pyruvate synthase  
EC 1.2.7.2 2-oxobutyrate synthase  
EC 1.2.7.3 2-oxoglutarate synthase  
EC 1.2.7.4 carbon-monoxide dehydrogenase (ferredoxin)  
EC 1.2.7.5 aldehyde ferredoxin oxidoreductase  
EC 1.2.7.6 glyceraldehyde-3-phosphate dehydrogenase (ferredoxin)  
EC 1.2.7.7 3-methyl-2-oxobutanoate dehydrogenase (ferredoxin)  
EC 1.2.7.8 indolepyruvate ferredoxin oxidoreductase  
EC 1.2.7.9 deleted, identical to EC 1.2.7.3

**EC 1.2.99 With other acceptors**

EC 1.2.99.1 now EC 1.17.99.4  
EC 1.2.99.2 carbon-monoxide dehydrogenase (acceptor)  
EC 1.2.99.3 aldehyde dehydrogenase (pyrroloquinoline-quinone)  
EC 1.2.99.4 formaldehyde dismutase  
EC 1.2.99.5 formylmethanofuran dehydrogenase  
EC 1.2.99.6 carboxylate reductase  
EC 1.2.99.7 aldehyde dehydrogenase (FAD-independent)

**EC 1.3 Acting on the CH-CH group of donors**

**EC 1.3.1 With NAD⁺ or NADP⁺ as acceptor**

EC 1.3.1.1 dihydrouracil dehydrogenase (NAD⁺)  
EC 1.3.1.2 dihydropyrimidine dehydrogenase (NADP⁺)  
EC 1.3.1.3 8β,3-oxosteroid 5β-reductase  
EC 1.3.1.4 cortisone α-reductase  
EC 1.3.1.5 cucurbitacin dβ-reductase  
EC 1.3.1.6 fumarate reductase (NADH)  
EC 1.3.1.7 meso-tartarate dehydrogenase  
EC 1.3.1.8 acyl-CoA dehydrogenase (NADP⁺)  
EC 1.3.1.9 enoyl-[acyl-carrier-protein] reductase (NADH)  
EC 1.3.1.10 enoyl-[acyl-carrier-protein] reductase (NADPH, B-specific)  
EC 1.3.1.11 2-coumarate reductase  
EC 1.3.1.12 prephenate dehydrogenase  
EC 1.3.1.13 prephenate dehydrogenase (NADP⁺)  
EC 1.3.1.14 orotate reductase (NADH)  
EC 1.3.1.15 orotate reductase (NADPH)  
EC 1.3.1.16 β-nitroacrylate reductase  
EC 1.3.1.17 3-methyleneoxindole reductase  
EC 1.3.1.18 kynurenate-7,8-dihydrodiol dehydrogenase  
EC 1.3.1.19 cis-1,2-dihydrobenzene-1,2-diol dehydrogenase  
EC 1.3.1.20 trans-1,2-dihydrobenzene-1,2-diol dehydrogenase  
EC 1.3.1.21 7-dehydrocholesterol reductase  
EC 1.3.1.22 cholestenone 5α-reductase  
EC 1.3.1.23 deleted now EC 1.3.1.3  
EC 1.3.1.24 biliverdin reductase  
EC 1.3.1.25 1,6-dihydroxycyclohexa-2,4-diene-1-carboxylate dehydrogenase  
EC 1.3.1.26 dihydrodipicolinate reductase  
EC 1.3.1.27 2-hexadecenal reductase  
EC 1.3.1.28 2,3-dihydro-2,3-dihydroxybenzoate dehydrogenase  
EC 1.3.1.29 cis-1,2-dihydro-1,2-dihydroxynaphthalene dehydrogenase  
EC 1.3.1.30 progesterone 5α-reductase  
EC 1.3.1.31 2-enoate reductase
EC 1.3.1.32 maleylacetate reductase
EC 1.3.1.33 protocatechuate dioxygenase
EC 1.3.1.34 2,4-dienoyl-CoA reductase (NADPH)
EC 1.3.1.35 phosphatidylylethanolamine desaturase
EC 1.3.1.36 geissoschizine dehydrogenase
EC 1.3.1.37 2,4-dienoyl-CoA reductase (NADPH)
EC 1.3.1.38 trans-2-enoyl-CoA reductase (NADPH)
EC 1.3.1.39 enoyl-[acyl-carrier-protein] reductase (NADPH, A-specific)
EC 1.3.1.40 2-hydroxy-6-oxo-6-phenylhexa-2,4-dienoate reductase
EC 1.3.1.41 xanthommatin reductase
EC 1.3.1.42 12-oxophytodienoate reductase
EC 1.3.1.43 arogenate dehydrogenase
EC 1.3.1.44 trans-2-enoyl-CoA reductase (NAD^+)
EC 1.3.1.45 2'-hydroxyisoflavone reductase
EC 1.3.1.46 biochanin-A reductase
EC 1.3.1.47 α-santonin 1,2-reductase
EC 1.3.1.48 15-oxo-prostaglandin 13-oxidase
EC 1.3.1.49 cis-3,4-dihydrophenanthrene-3,4-diol dehydrogenase
EC 1.3.1.50 now EC 1.1.1.252
EC 1.3.1.51 2'-hydroxydaidzein reductase
EC 1.3.1.52 2-methyl-branched-chain-enoyl-CoA reductase
EC 1.3.1.53 (3S,4R)-3,4-dihydroxycyclohexa-1,5-diene-1,4-dicarboxylate dehydrogenase
EC 1.3.1.54 precorrin-6A reductase
EC 1.3.1.55 now EC 1.3.1.25
EC 1.3.1.56 cis-2,3-dihydrodimethylphenol-2,3-diol dehydrogenase
EC 1.3.1.57 phloroglucinol reductase
EC 1.3.1.58 2,3-dihydroxy-2,3-dihydro-p-cumarate dehydrogenase
EC 1.3.1.59 deleted entry.
EC 1.3.1.60 dibenzo[b,f]xanthene-9,10-dihydrodiol dehydrogenase
EC 1.3.1.61 terephthalate 1,2-cis-dihydroidiol dehydrogenase
EC 1.3.1.62 pimeloyl-CoA dehydrogenase
EC 1.3.1.63 2,4-dichlorobenzoyl-CoA reductase
EC 1.3.1.64 phthalate 4,5-cis-dihydroidiol dehydrogenase
EC 1.3.1.65 5,6-dihydroxy-3-methyl-2-oxo-1,2,5,6-tetrahydroquinoline dehydrogenase
EC 1.3.1.66 cis-dihydroxyacetate dehydrogenase
EC 1.3.1.67 cis-1,2-dihydroxycyclohexa-3,5-diene-1-carboxylate dehydrogenase
EC 1.3.1.68 1,2-dihydroxycyclohexa-3,5-diene-1-carboxylate dehydrogenase
EC 1.3.1.69 zeatin reductase
EC 1.3.1.70 8^14-sterol reductase
EC 1.3.1.71 8^24(241)-sterol reductase
EC 1.3.1.72 8^24-sterol reductase
EC 1.3.1.73 1,2-dihydroxyomilenine reductase
EC 1.3.1.74 2-alkenal reductase
EC 1.3.1.75 divinyl chlorophyllide a 8-vinyl-reductase
EC 1.3.1.76 precorrin-2 dehydrogenase
EC 1.3.1.77 anthocyanidin reductase
EC 1.3.1.78 arogenate dehydrogenase (NADP^+)
EC 1.3.1.79 arogenate dehydrogenase [NAD(P)^+]

**EC 1.3.2 With a cytochrome as acceptor**

EC 1.3.2.1 now EC 1.3.99.2
EC 1.3.2.2 now EC 1.3.99.3
EC 1.3.2.3 galactonolactone dehydrogenase

**EC 1.3.3 With oxygen as acceptor**
EC 1.3.3.1 dihydroorotate oxidase
EC 1.3.3.2 now EC 1.14.21.6
EC 1.3.3.3 coproporphyrinogen oxidase
EC 1.3.3.4 protoporphyrinogen oxidase
EC 1.3.3.5 bilirubin oxidase
EC 1.3.3.6 acyl-CoA oxidase
EC 1.3.3.7 dihydrouracil oxidase
EC 1.3.3.8 tetrahydroberberine oxidase
EC 1.3.3.9 secolloganin synthase
EC 1.3.3.10 tryptophan α,β-oxidase
EC 1.3.3.11 pyrroloquinoline-quinone synthase

EC 1.3.5 With a quinone or related compound as acceptor
EC 1.3.5.1 succinate dehydrogenase (ubiquinone)

EC 1.3.7 With an iron-sulfur protein as acceptor
EC 1.3.7.1 6-hydroxynicotinamide reductase
EC 1.3.7.2 15,16-dihydrobacteriochlorophyll:ferredoxin oxidoreductase
EC 1.3.7.3 phycoerythrobilin:ferredoxin oxidoreductase
EC 1.3.7.4 phycocromobilin:ferredoxin oxidoreductase
EC 1.3.7.5 phycocyanobilin:ferredoxin oxidoreductase

EC 1.3.99 With other acceptors
EC 1.3.99.1 succinate dehydrogenase
EC 1.3.99.2 butyryl-CoA dehydrogenase
EC 1.3.99.3 acyl-CoA dehydrogenase
EC 1.3.99.4 3-oxosteroid 1-dehydrogenase
EC 1.3.99.5 3-oxo-5α-steroid 4-dehydrogenase
EC 1.3.99.6 3-oxo-5β-steroid 4-dehydrogenase
EC 1.3.99.7 glutaryl-CoA dehydrogenase
EC 1.3.99.8 2-furoyl-CoA dehydrogenase
EC 1.3.99.9 now EC 1.21.99.1
EC 1.3.99.10 isovaleryl-CoA dehydrogenase
EC 1.3.99.11 dihydroorotate dehydrogenase
EC 1.3.99.12 2-methylacyl-CoA dehydrogenase
EC 1.3.99.13 long-chain-acyl-CoA dehydrogenase
EC 1.3.99.14 cyclohexanone dehydrogenase
EC 1.3.99.15 benzoyl-CoA reductase
EC 1.3.99.16 isoquinoline 1-oxidoreductase
EC 1.3.99.17 quinoline 2-oxidoreductase
EC 1.3.99.18 quinaldine 4-oxidoreductase
EC 1.3.99.19 quinoline-4-carboxylate 2-oxidoreductase
EC 1.3.99.20 4-hydroxybenzoyl-CoA reductase
EC 1.3.99.21 (R)-benzylsuccinyl-CoA dehydrogenase
EC 1.3.99.22 coproporphyrinogen dehydrogenase
EC 1.3.99.23 all-trans-retinol 13,14-reductase

EC 1.4 Acting on the CH-NH₂ group of donors

EC 1.4.1.1 alanine dehydrogenase
EC 1.4.1.2 glutamate dehydrogenase
EC 1.4.1.3 glutamate dehydrogenase [NAD(P)⁺]
EC 1.4.1.4 glutamate dehydrogenase (NADP⁺)
EC 1.4.1.5 L-amino-acid dehydrogenase
EC 1.4.1.6 deleted, included in EC 1.4.4.1
EC 1.4.1.7 serine 2-dehydrogenase
EC 1.4.1.8 valine dehydrogenase (NADP⁺)
EC 1.4.1.9 leucine dehydrogenase
EC 1.4.1.10 glycine dehydrogenase
EC 1.4.1.11 L-erythro-3,5-diaminohexanoate dehydrogenase
EC 1.4.1.12 2,4-diaminopimelate dehydrogenase
EC 1.4.1.13 glutamate synthase (NADPH)
EC 1.4.1.14 glutamate synthase (NADH)
EC 1.4.1.15 lysine dehydrogenase
EC 1.4.1.16 diaminopimelate dehydrogenase
EC 1.4.1.17 N-methylalanine dehydrogenase
EC 1.4.1.18 lysine 6-dehydrogenase
EC 1.4.1.19 tryptophan dehydrogenase
EC 1.4.1.20 phenylalanine dehydrogenase
EC 1.4.1.21 aspartate dehydrogenase
EC 1.4.1.22 deleted

**EC 1.4.2 With a cytochrome as acceptor**
EC 1.4.2.1 glycine dehydrogenase (cytochrome)

**EC 1.4.3 With oxygen as acceptor**

EC 1.4.3.1 D-aspartate oxidase
EC 1.4.3.2 L-amino-acid oxidase
EC 1.4.3.3 D-amino-acid oxidase
EC 1.4.3.4 amine oxidase (flavin-containing)
EC 1.4.3.5 pyridoxal 5'-phosphate synthase
EC 1.4.3.6 amine oxidase (copper-containing)
EC 1.4.3.7 D-glutamate oxidase
EC 1.4.3.8 ethanolamine oxidase
EC 1.4.3.9 deleted, included in EC 1.4.3.4
EC 1.4.3.10 putrescine oxidase
EC 1.4.3.11 L-glutamate oxidase
EC 1.4.3.12 cyclohexylamine oxidase
EC 1.4.3.13 protein-lysine 6-oxidase
EC 1.4.3.14 L-lysine oxidase
EC 1.4.3.15 D-glutamate(D-aspartate) oxidase
EC 1.4.3.16 L-aspartate oxidase
EC 1.4.3.17 now EC 1.3.3.10
EC 1.4.3.18 deleted, not approved
EC 1.4.3.19 glycine oxidase
EC 1.4.3.20 L-lysine 6-oxidase

**EC 1.4.4 With a disulfide as acceptor**
EC 1.4.4.1 now EC 1.21.4.1
*EC 1.4.4.2 glycine dehydrogenase (decarboxylating)

**EC 1.4.7 With an iron-sulfur protein as acceptor**
EC 1.4.7.1 glutamate synthase (ferredoxin)

**EC 1.4.99 With other acceptors**

EC 1.4.99.1 D-amino-acid dehydrogenase
EC 1.4.99.2 taurine dehydrogenase
EC 1.4.99.3 amine dehydrogenase
EC 1.4.99.4 aralkylamine dehydrogenase
EC 1.4.99.5 glycine dehydrogenase (cyanide-forming)

EC 1.5 Acting on the CH-NH group of donors

**EC 1.5.1 With NAD⁺ or NADP⁺ as acceptor**

EC 1.5.1.1 pyrroline-2-carboxylate reductase
EC 1.5.1.2 pyrroline-5-carboxylate reductase
EC 1.5.1.3 dihydrofolate reductase
EC 1.5.1.4 deleted, included in EC 1.5.1.3
EC 1.5.1.5 methylenetetrahydrofolate dehydrogenase (NADP⁺)
EC 1.5.1.6 formyltetrahydrofolate dehydrogenase
EC 1.5.1.7 saccharopine dehydrogenase (NAD⁺, L-lysine-forming)
EC 1.5.1.8 saccharopine dehydrogenase (NADP⁺, L-lysine-forming)
EC 1.5.1.9 saccharopine dehydrogenase (NAD⁺, L-glutamate-forming)
EC 1.5.1.10 saccharopine dehydrogenase (NADP⁺, L-glutamate-forming)
EC 1.5.1.11 D-octopine dehydrogenase
EC 1.5.1.12 1-pyrroline-5-carboxylate dehydrogenase
EC 1.5.1.13 now EC 1.17.1.5
EC 1.5.1.14 deleted, included in EC 1.5.1.21
EC 1.5.1.15 methylenetetrahydrofolate dehydrogenase (NAD⁺)
EC 1.5.1.16 D-lysopine dehydrogenase
EC 1.5.1.17 alanopine dehydrogenase
EC 1.5.1.18 ephedrine dehydrogenase
EC 1.5.1.19 D-nopaline dehydrogenase
EC 1.5.1.20 methylenetetrahydrofolate reductase [NAD(P)H]
EC 1.5.1.21 δ'-piperidine-2-carboxylate reductase
EC 1.5.1.22 strombine dehydrogenase
EC 1.5.1.23 tauropine dehydrogenase
EC 1.5.1.24 N⁴-(carboxyethyl)ornithine synthase
EC 1.5.1.25 thiomorpholine-carboxylate dehydrogenase
EC 1.5.1.26 β-alanopine dehydrogenase
EC 1.5.1.27 1,2-dehydroreticulinium reductase (NADPH)
EC 1.5.1.28 opine dehydrogenase
EC 1.5.1.29 FMN reductase
EC 1.5.1.30 flavin reductase
EC 1.5.1.31 berberine reductase
EC 1.5.1.32 vomilenine reductase
EC 1.5.1.33 pteridine reductase
EC 1.5.1.34 6,7-dihydropteridine reductase
EC 1.5.1.35 1-pyrroline dehydrogenase

**EC 1.5.3 With oxygen as acceptor**

EC 1.5.3.1 sarcosine oxidase
EC 1.5.3.2 N-methyl-L-αmino-acid oxidase
EC 1.5.3.3 deleted
EC 1.5.3.4 N⁶-methyl-lysine oxidase
EC 1.5.3.5 (S)-6-hydroxynicotine oxidase
EC 1.5.3.6 (R)-6-hydroxynicotine oxidase
EC 1.5.3.7 L-pipecolate oxidase
EC 1.5.3.8 deleted, included in EC 1.3.3.8
EC 1.5.3.9 now EC 1.21.3.3
EC 1.5.3.10 dimethylglycine oxidase
EC 1.5.3.11 polyamine oxidase
EC 1.5.3.12 dihydrobenzophenanthidine oxidase
EC 1.5.4 With a disulfide as acceptor
EC 1.5.4.1 pyrimidodiazepine synthase
EC 1.5.5 With a quinone or similar compound as acceptor
EC 1.5.5.1 electron-transferring-flavoprotein dehydrogenase
EC 1.5.7 With an iron-sulfur protein as acceptor
EC 1.5.7.1 methylenetetrahydrofolate reductase (ferredoxin)
EC 1.5.8 With a flavin as acceptor
EC 1.5.8.1 dimethylamine dehydrogenase
EC 1.5.8.2 trimethylamine dehydrogenase
EC 1.5.99 With other acceptors
EC 1.5.99.1 sarcosine dehydrogenase
EC 1.5.99.2 dimethylglycine dehydrogenase
EC 1.5.99.3 L-pipecolate dehydrogenase
EC 1.5.99.4 nicotine dehydrogenase
EC 1.5.99.5 methylnitrate dehydrogenase
EC 1.5.99.6 spermidine dehydrogenase
EC 1.5.99.7 now EC 1.5.8.2
EC 1.5.99.8 proline dehydrogenase
EC 1.5.99.9 methylenetetrahydromethanopterin dehydrogenase
EC 1.5.99.10 now EC 1.5.8.1
EC 1.5.99.11 5,10-methylenetetrahydromethanopterin reductase
EC 1.5.99.12 cytokinin dehydrogenase

EC 1.6 Acting on NADH or NADPH

EC 1.6.1 With NAD$^+$ or NADP$^+$ as acceptor

EC 1.6.1.1 NAD(P)$^+$ transhydrogenase (B-specific)
EC 1.6.1.2 NAD(P)$^+$ transhydrogenase (AB-specific)
EC 1.6.2 With a heme protein as acceptor
EC 1.6.2.1 now EC 1.6.99.3
EC 1.6.2.2 cytochrome-b$_5$ reductase
EC 1.6.2.3 deleted
EC 1.6.2.4 NADPH—hemoprotein reductase
EC 1.6.2.5 NADPH—cytochrome-c$_5$ reductase
EC 1.6.2.6 leghemoglobin reductase
EC 1.6.3 With oxygen as acceptor
EC 1.6.3.1 NAD(P)H oxidase
EC 1.6.4 With a disulfide as acceptor
EC 1.6.4.1 now EC 1.8.1.6
EC 1.6.4.2 now EC 1.8.1.7
EC 1.6.4.3 now EC 1.8.1.4
EC 1.6.4.4 now EC 1.8.1.8
EC 1.6.4.5 now EC 1.8.1.9
EC 1.6.4.6 now EC 1.8.1.10
EC 1.6.4.7 now EC 1.8.1.11
EC 1.6.4.8 now EC 1.8.1.12
EC 1.6.4.9 now EC 1.8.1.13
EC 1.6.4.10 now EC 1.8.1.14
EC 1.6.5 With a quinone or similar compound as acceptor
EC 1.6.5.1 deleted
EC 1.6.5.2 NAD(P)H dehydrogenase (quinone)
EC 1.6.5.3 NADH dehydrogenase (ubiquinone)
EC 1.6.5.4 monodehydroascorbate reductase (NADH)
EC 1.6.5.5 NADPH:quinone reductase
EC 1.6.5.6 $p$-benzoquinone reductase (NADPH)
EC 1.6.5.7 2-hydroxy-1,4-benzoquinone reductase

EC 1.6.6 With a nitrogenous group as acceptor
EC 1.6.6.1 now EC 1.7.1.1
EC 1.6.6.2 now EC 1.7.1.2
EC 1.6.6.3 now EC 1.7.1.3
EC 1.6.6.4 now EC 1.7.1.4
EC 1.6.6.5 now EC 1.7.99.3
EC 1.6.6.6 now EC 1.7.1.5
EC 1.6.6.7 now EC 1.7.1.6
EC 1.6.6.8 now EC 1.7.1.7
EC 1.6.6.9 trimethylamine-N-oxide reductase
EC 1.6.6.10 now EC 1.7.1.9
EC 1.6.6.11 now EC 1.7.1.10
EC 1.6.6.12 now EC 1.7.1.11
EC 1.6.6.13 now EC 1.7.1.12

EC 1.6.7 With a iron-sulfur protein as acceptor
EC 1.6.7.1 now EC 1.18.1.2
EC 1.6.7.2 now EC 1.18.1.1

EC 1.6.8 With a flavin as acceptor
EC 1.6.8.1 now EC 1.5.1.29
EC 1.6.8.2 now EC 1.5.1.30

EC 1.6.99 With other acceptors
EC 1.6.99.1 NADPH dehydrogenase
EC 1.6.99.2 now EC 1.6.5.2
EC 1.6.99.3 NADH dehydrogenase
EC 1.6.99.4 now EC 1.18.1.2
EC 1.6.99.5 NADH dehydrogenase (quinone)
EC 1.6.99.6 NADPH dehydrogenase (quinone)
EC 1.6.99.7 now EC 1.5.1.34
EC 1.6.99.8 now EC 1.16.1.3
EC 1.6.99.9 now EC 1.16.1.4
EC 1.6.99.10 deleted, included in EC 1.6.99.7
EC 1.6.99.11 now EC 1.16.1.5
EC 1.6.99.12 now EC 1.16.1.6
EC 1.6.99.13 now EC 1.16.1.7

EC 1.7 Acting on other nitrogenous compounds as donors

EC 1.7.1 With NAD$^+$ or NADP$^+$ as acceptor

EC 1.7.1.1 nitrate reductase (NADH)
EC 1.7.1.2 nitrate reductase [NAD(P)H]
EC 1.7.1.3.1 nitrate reductase (NADPH)
EC 1.7.1.4 nitrite reductase [NAD(P)H]
EC 1.7.1.6 GMP reductase
EC 1.7.1.7 azobenzene reductase
EC 1.7.1.9 nitroquinoline-N-oxide reductase

EC 1.7.1.8 Deleted entry: withdrawn in the light of further information on the acceptor
EC 1.7.1.10 hydroxylamine reductase (NADH)
EC 1.7.1.11 4-(dimethylamino)phenylazoxybenzene reductase
EC 1.7.1.12 N-hydroxy-2-acetamidofluorene reductase
EC 1.7.1.13 queuine reductase

**EC 1.7.2 With a cytochrome as acceptor**
EC 1.7.2.1 nitrite reductase (NO-forming)
EC 1.7.2.2 nitrite reductase (cytochrome; ammonia-forming)
EC 1.7.2.3 trimethylamine-N-oxide reductase (cytochrome c)

**EC 1.7.3 With oxygen as acceptor**
EC 1.7.3.1 nitroethane oxidase
EC 1.7.3.2 acetylindoxyl oxidase
EC 1.7.3.3 urate oxidase
EC 1.7.3.4 hydroxylamine oxidase
EC 1.7.3.5 3-aci-nitropropionate oxidase

**EC 1.7.7 With an iron-sulfur protein as acceptor**
EC 1.7.7.1 ferredoxin—nitrite reductase
EC 1.7.7.2 ferredoxin—nitrate reductase

**EC 1.7.99 With other acceptors**
EC 1.7.99.1 hydroxylamine reductase
EC 1.7.99.2 deleted
EC 1.7.99.3 included with EC 1.7.2.1
EC 1.7.99.4 nitrate reductase
EC 1.7.99.5 deleted, now included with EC 1.5.1.20
EC 1.7.99.6 nitrous-oxide reductase
EC 1.7.99.7 nitric-oxide reductase
EC 1.7.99.8 hydroxylamine oxidoreductase

**EC 1.8 Acting on a sulfur group of donors**

**EC 1.8.1 With NAD⁺ or NADP⁺ as acceptor**
EC 1.8.1.1 deleted
EC 1.8.1.2 sulfite reductase (NADPH)
EC 1.8.1.3 hypotaurine dehydrogenase
EC 1.8.1.4 dihydrolipoyl dehydrogenase
EC 1.8.1.5 2-oxopropyl-CoM reductase (carboxylating)
EC 1.8.1.6 cystine reductase
EC 1.8.1.7 glutathione-disulfide reductase
EC 1.8.1.8 protein-disulfide reductase
EC 1.8.1.9 thioredoxin-disulfide reductase
EC 1.8.1.10 CoA-glutathione reductase
EC 1.8.1.11 asparagusic reductase
EC 1.8.1.12 trypanothione-disulfide reductase
EC 1.8.1.13 bis-γ-glutamyleystine reductase
EC 1.8.1.14 CoA-disulfide reductase
EC 1.8.1.15 mycothione reductase

**EC 1.8.2 With a cytochrome as acceptor**
EC 1.8.2.1 sulfite dehydrogenase
EC 1.8.2.2 thiosulfate dehydrogenase

**EC 1.8.3 With oxygen as acceptor**
EC 1.8.3.1 sulfite oxidase
EC 1.8.3.2 thiol oxidase
EC 1.8.3.3 glutathione oxidase
EC 1.8.3.4 methanethiol oxidase
EC 1.8.3.5 prenylcysteine oxidase
EC 1.8.4.1 With a disulfide as acceptor
   EC 1.8.4.1 glutathione—homocysteine transhydrogenase
   EC 1.8.4.2 protein-disulfide reductase (glutathione)
   EC 1.8.4.3 glutathione—CoA-glutathione transhydrogenase
   EC 1.8.4.4 glutathione—cystine transhydrogenase
   EC 1.8.4.5 now EC 1.8.4.13 and EC 1.8.4.14
   EC 1.8.4.6 now EC 1.8.4.11
   EC 1.8.4.7 enzyme-thiol transhydrogenase (glutathione-disulfide)
   EC 1.8.4.8 phosphoadenyl-sulfate reductase (thioredoxin)
   EC 1.8.4.9 adenyllyl-sulfate reductase (glutathione)
   EC 1.8.4.10 adenyllyl-sulfate reductase (thioredoxin)
   EC 1.8.4.11 peptide-methionine (S)-S-oxide reductase
   EC 1.8.4.12 peptide-methionine (R)-S-oxide reductase
   EC 1.8.4.13 L-methionine (S)-S-oxide reductase
   EC 1.8.4.14 L-methionine (R)-S-oxide reductase
EC 1.8.5 With a quinone or similar compound as acceptor
   EC 1.8.5.1 glutathione dehydrogenase (ascorbate)
   EC 1.8.5.2 thiosulfate dehydrogenase (quinone)
EC 1.8.6 With an nitrogenous group as acceptor
   EC 1.8.6.1 deleted, included in EC 2.5.1.18
EC 1.8.7 With an iron-sulfur protein as acceptor
   EC 1.8.7.1 sulfite reductase (ferredoxin)
EC 1.8.98 With other, known, acceptors
   EC 1.8.98.1 CoB—CoM heterodisulfide reductase
   EC 1.8.98.2 sulfiredoxin
EC 1.8.99 With other acceptors
   EC 1.8.99.1 sulfite reductase
   EC 1.8.99.2 adenyllyl-sulfate reductase
   EC 1.8.99.3 hydrogensulfite reductase
   EC 1.8.99.4 now EC 1.8.4.8

EC 1.9 Acting on a heme group of donors

EC 1.9.3 With oxygen as acceptor
   EC 1.9.3.1 cytochrome-c oxidase
   EC 1.9.3.2 included with EC 1.7.2.1
EC 1.9.6 With a nitrogenous group as acceptor
   EC 1.9.6.1 nitrate reductase (cytochrome)
EC 1.9.99 With other acceptors
   EC 1.9.99.1 iron—cytochrome-c reductase

EC 1.10 Acting on diphenols and related substances as donors

EC 1.10.1 With NAD⁺ or NADP⁺ as acceptor
   EC 1.10.1.1 trans-acenaphthene-1,2-diol dehydrogenase
EC 1.10.2 With a cytochrome as acceptor
   EC 1.10.2.1 L-ascorbate—cytochrome-‌b₅ reductase
   EC 1.10.2.2 ubiquinol—cytochrome-c reductase
EC 1.10.3 With oxygen as acceptor
   EC 1.10.3.1 catechol oxidase
   EC 1.10.3.2 laccase
EC 1.10.3.3 L-ascorbate oxidase
EC 1.10.3.4 o-aminophenol oxidase
EC 1.10.3.5 3-hydroxyanthranilate oxidase
EC 1.10.3.6 rifamycin-B oxidase
EC 1.10.3.7 now EC 1.21.3.4
EC 1.10.3.8 now EC 1.21.3.5

EC 1.10.99 With other acceptors
EC 1.10.99.1 plastoquinol—plastocyanin reductase
EC 1.10.99.2 ribosylhydronicotinamide dehydrogenase (quinone)
EC 1.10.99.3 violaxanthin de-epoxidase

EC 1.11 Acting on a peroxide as acceptor

EC 1.11.1 Peroxidases

EC 1.11.1.1 NADH peroxidase
EC 1.11.1.2 NADPH peroxidase
EC 1.11.1.3 fatty-acid peroxidase
EC 1.11.1.4 now EC 1.13.11.11
EC 1.11.1.5 cytochrome-c peroxidase
EC 1.11.1.6 catalase
EC 1.11.1.7 peroxidase
EC 1.11.1.8 iodide peroxidase
EC 1.11.1.9 glutathione peroxidase
EC 1.11.1.10 chloride peroxidase
EC 1.11.1.11 L-ascorbate peroxidase
EC 1.11.1.12 phospholipid-hydroperoxide glutathione peroxidase
EC 1.11.1.13 manganese peroxidase
EC 1.11.1.14 lignin peroxidase
EC 1.11.1.15 peroxiredoxin
EC 1.11.1.16 versatile peroxidase

EC 1.12 Acting on hydrogen as donor

EC 1.12.1 With NAD\(^+\) or NADP\(^+\) as acceptor

EC 1.12.1.1 now EC 1.18.99.1
EC 1.12.1.2 hydrogen dehydrogenase
EC 1.12.1.3 hydrogen dehydrogenase (NAD\(^+\))

EC 1.12.2 With a cytochrome as acceptor
EC 1.12.2.1 cytochrome-c\(_5\) hydrogenase

EC 1.12.5 With a quinone or similar compound as acceptor
EC 1.12.5.1 hydrogen:quinone oxidoreductase

EC 1.12.7 With an iron-sulfur protein as acceptor
EC 1.12.7.1 now EC 1.18.99.1
EC 1.12.7.2 ferredoxin hydrogenase

EC 1.12.98 With other known acceptors
EC 1.12.98.1 coenzyme F\(_{420}\) hydrogenase
EC 1.12.98.2 5,10-methylenetetrahydromethanopterin hydrogenase
EC 1.12.98.3 Methanosarcina-phenazine hydrogenase

EC 1.12.99 With other acceptors
EC 1.12.99.1 now EC 1.12.98.1
EC 1.12.99.2 deleted, composed of EC 1.12.98.3 and EC 1.8.98.1
EC 1.12.99.3 now EC 1.12.5.1
EC 1.12.99.4 now EC 1.12.98.2
EC 1.12.99.5 deleted, identical to EC 1.13.11.47
EC 1.12.99.6 hydrogenase (acceptor)

EC 1.13 Acting on single donors with incorporation of molecular oxygen (oxygenases)

EC 1.13.11 With incorporation of two atoms of oxygen

EC 1.13.11.1 catechol 1,2-dioxygenase
EC 1.13.11.2 catechol 2,3-dioxygenase
EC 1.13.11.3 protocatechuate 3,4-dioxygenase
EC 1.13.11.4 gentisate 1,2-dioxygenase
EC 1.13.11.5 homogentisate 1,2-dioxygenase
EC 1.13.11.6 3-hydroxyanthranilate 3,4-dioxygenase
EC 1.13.11.7 deleted
EC 1.13.11.8 protocatechuate 4,5-dioxygenase
EC 1.13.11.9 2,5-dihydroxypyridine 5,6-dioxygenase
EC 1.13.11.10 7,8-dihydroxykynurenate 8,8a-dioxygenase
EC 1.13.11.11 tryptophan 2,3-dioxygenase
EC 1.13.11.12 lipoxygenase
EC 1.13.11.13 ascorbate 2,3-dioxygenase
EC 1.13.11.14 2,3-dihydroxybenzoate 3,4-dioxygenase
EC 1.13.11.15 3,4-dihydroxyphenylacetate 2,3-dioxygenase
EC 1.13.11.16 3-carboxyethylcatechol 2,3-dioxygenase
EC 1.13.11.17 indole 2,3-dioxygenase
EC 1.13.11.18 sulfur dioxygenase
EC 1.13.11.19 cysteamine dioxygenase
EC 1.13.11.20 cysteine dioxygenase
EC 1.13.11.21 now EC 1.14.99.36
EC 1.13.11.22 caffeine 3,4-dioxygenase
EC 1.13.11.23 2,3-dihydroxyindole 2,3-dioxygenase
EC 1.13.11.24 quercetin 2,3-dioxygenase
EC 1.13.11.25 3,4-dihydroxy-9,10-secoandrosta-1,3,5(10)-triene-9,17-dione 4,5-dioxygenase
EC 1.13.11.26 peptidotryptophan 2,3-dioxygenase
EC 1.13.11.27 4-hydroxyphenylpyruvate dioxygenase
EC 1.13.11.28 2,3-dihydroxybenzoate 2,3-dioxygenase
EC 1.13.11.29 stizolobate synthase
EC 1.13.11.30 stizolobinate synthase
EC 1.13.11.31 arachidonate 12-lipoxygenase
EC 1.13.11.32 2-nitropropane dioxygenase
EC 1.13.11.33 arachidonate 15-lipoxygenase
EC 1.13.11.34 arachidonate 5-lipoxygenase
EC 1.13.11.35 pyrogallol 1,2-oxygenase
EC 1.13.11.36 chloridazon-catechol dioxygenase
EC 1.13.11.37 hydroxyquinol 1,2-dioxygenase
EC 1.13.11.38 1-hydroxy-2-naphthoate 1,2-dioxygenase
EC 1.13.11.39 biphenyl-2,3-diol 1,2-dioxygenase
EC 1.13.11.40 arachidonate 8-lipoxygenase
EC 1.13.11.41 2,4-dihydroxyacetophenone dioxygenase
EC 1.13.11.42 deleted
EC 1.13.11.43 lignostilbene αβ-dioxygenase
EC 1.13.11.44 linoleate diol synthase
EC 1.13.11.45 linoleate 11-lipoxygenase
EC 1.13.11.46 4-hydroxymandelate synthase
EC 1.13.11.47 3-hydroxy-4-oxoquinoline 2,4-dioxygenase
EC 1.13.11.48 3-hydroxy-2-methyl-quinolin-4-one 2,4-dioxygenase
EC 1.13.11.49 chlorite O₂-lyase
EC 1.13.11.50 acetylacetone-cleaving enzyme
EC 1.13.11.51 9-cis-epoxycarotenoid dioxygenase
EC 1.13.11.52 indoleamine 2,3-dioxygenase
EC 1.13.11.53 acireductone dioxygenase (Ni²⁺-requiring)
EC 1.13.11.54 acireductone dioxygenase [iron(II)-requiring]
EC 1.13.11.55 sulfur oxygenase/reductase

EC 1.13.12 With incorporation of one atom of oxygen (internal monooxygenases or internal mixed function oxidases)
EC 1.13.12.1 arginine 2-monooxygenase
EC 1.13.12.2 lysine 2-monooxygenase
EC 1.13.12.3 tryptophan 2-monooxygenase
EC 1.13.12.4 lactate 2-monooxygenase
EC 1.13.12.5 Renilla-luciferin 2-monooxygenase
EC 1.13.12.6 Cypridina-luciferin 2-monooxygenase
EC 1.13.12.7 Photorinus-luciferin 4-monooxygenase (ATP-hydrolysing)
EC 1.13.12.8 Wataseinia-luciferin 2-monooxygenase
EC 1.13.12.9 phenylalanine 2-monooxygenase
EC 1.13.12.10 lysine 6-monooxygenase
EC 1.13.12.11 now EC 1.14.13.8
EC 1.13.12.12 apo-β-carotenoid-14',13'-dioxygenase
EC 1.13.12.13 Oplophorus-luciferin 2-monooxygenase
EC 1.13.12.14 chlorophyllide a oxygenase

EC 1.13.99 Miscellaneous
EC 1.13.99.1 inositol oxygenase
EC 1.13.99.2 now EC 1.14.12.10
EC 1.13.99.3 tryptophan 2'-dioxygenase
EC 1.13.99.4 now EC 1.14.12.9
EC 1.13.99.5 now EC 1.13.11.47

EC 1.14 Acting on paired donors, with incorporation or reduction of molecular oxygen

EC 1.14.11 With 2-oxoglutarate as one donor, and incorporation of one atom each of oxygen into both donors

EC 1.14.11.1 γ-butyrobetaine dioxygenase
EC 1.14.11.2 procollagen-proline dioxygenase
EC 1.14.11.3 pyrimidine-deoxynucleoside 2'-dioxygenase
EC 1.14.11.4 procollagen-lysine 5-dioxygenase
EC 1.14.11.5 deleted, included in EC 1.14.11.6
EC 1.14.11.6 thymine dioxygenase
EC 1.14.11.7 procollagen-proline 3-dioxygenase
EC 1.14.11.8 trimethyllysine dioxygenase
EC 1.14.11.9 flavanone 3-dioxygenase
EC 1.14.11.10 pyrimidine-deoxynucleoside 1'-dioxygenase
EC 1.14.11.11 hyoscyamine (6ß)-dioxygenase
EC 1.14.11.12 gibberellin-44 dioxygenase
EC 1.14.11.13 gibberellin 2β-dioxygenase
EC 1.14.6β-hydroxyhyoscyamine epoxidase
EC 1.14.11.15 gibberellin 3β-dioxygenase
EC 1.14.11.16 peptide-aspartate β-dioxygenase
EC 1.14.11.17 taurine dioxygenase
EC 1.14.11.18 phytanoyl-CoA dioxygenase
EC 1.14.11.19 leucocyanidin oxygenase
EC 1.14.11.20 deacetoxyvinodoline 4-hydroxylase
EC 1.14.11.21 clavaminate synthase
EC 1.14.11.22 flavone synthase
EC 1.14.11.23 flavonol synthase
EC 1.14.11.24 2'-deoxymugineic-acid 2'-dioxygenase
EC 1.14.11.25 mugineic-acid 3-dioxygenase
EC 1.14.11.26 deacetoxycephalosporin-C hydroxylase
EC 1.14.11.27 [histone-H3]-lysine-36 demethylase
EC 1.14.11.28 proline 3-hydroxylase

EC 1.14.12 With NADH or NADPH as one donor, and incorporation of two atoms of oxygen into one donor
EC 1.14.12.1 anthranilate 1,2-dioxygenase (deaminating, decarboxylating)
EC 1.14.12.3 benzene 1,2-dioxygenase
EC 1.14.12.4 3-hydroxy-2-methylpyridinecarboxylate dioxygenase
EC 1.14.12.5 5-pyridoxate dioxygenase
EC 1.14.12.7 phthalate 4,5-dioxygenase
EC 1.14.12.8 4-sulfobenzoate 3,4-dioxygenase
EC 1.14.12.9 4-chloropheny lacetate 3,4-dioxygenase
EC 1.14.12.10 benzoate 1,2-dioxygenase
EC 1.14.12.11 toluene dioxygenase
EC 1.14.12.12 naphthalene 1,2-dioxygenase
EC 1.14.12.13 2-chlorobenzoate 1,2-dioxygenase
EC 1.14.12.14 2-aminobenzenesulfonate 2,3-dioxygenase
EC 1.14.12.15 terephthalate 1,2-dioxygenase
EC 1.14.12.16 2-hydroxyquinoline 5,6-dioxygenase
EC 1.14.12.17 nitric oxide dioxygenase
EC 1.14.12.18 biphenyl 2,3-dioxygenase
EC 1.14.12.19 3-phenylpropionate dioxygenase

EC 1.14.13 With NADH or NADPH as one donor, and incorporation of one atom of oxygen
EC 1.14.13.1 salicylate 1-monoxygenase
EC 1.14.13.2 4-hydroxyb enzoate 3-monoxygenase
EC 1.14.13.3 4-hydroxyphenylacetate 3-monoxygenase
EC 1.14.13.4 mehlo lactate 3-monoxygenase
EC 1.14.13.5 imidazoleacetate 4-monoxygenase
EC 1.14.13.6 o rcinol 2-monoxygenase
EC 1.14.13.7 phenol 2-monoxygenase
EC 1.14.13.8 flavin-containing monoxygenase
EC 1.14.13.9 kynurenine 3-monoxygenase
EC 1.14.13.10 2,6-dihydroxy pyridine 3-monoxygenase
EC 1.14.13.11 trans-cinnamate 4-monoxygenase
EC 1.14.13.12 benzoate 4-monoxygenase
EC 1.14.13.13 calcidiol 1-monoxygenase
EC 1.14.13.14 trans-cinnamate 2-monoxygenase
EC 1.14.13.15 cholestanetriol 26-monoxygenase
EC 1.14.13.16 cyclopentanone monoxygenase
EC 1.14.13.17 cholesterol 7α-monoxygenase
EC 1.14.13.18 4-hydroxyphenylacetate 1-monoxygenase
EC 1.14.13.19 taxifolin 8-monoxygenase
EC 1.14.13.20 2,4-dichlorophenol 6-monoxygenase
EC 1.14.13.21 flavonoid 3′-monooxygenase
EC 1.14.13.22 cyclohexanone monoxygenase
EC 1.14.13.23 3-hydroxybenzoate 4-monoxygenase
EC 1.14.13.24 3-hydroxybenzoate 6-monoxygenase
EC 1.14.13.25 methane monoxygenase
EC 1.14.13.26 phosphatidylcholine 12-monoxygenase
EC 1.14.13.27 4-aminobenzoate 1-monoxygenase
EC 1.14.13.28 3,9-dihydroxypterocarpan 6α-monoxygenase
EC 1.14.13.29 4-nitrophenol 2-monoxygenase
EC 1.14.13.30 leukotriene-B4 20-monoxygenase
EC 1.14.13.31 2-nitrophenol 2-monoxygenase
EC 1.14.13.32 albendazole monoxygenase
EC 1.14.13.33 4-hydroxybenzoate 3-monoxygenase [NAD(P)H] 
EC 1.14.13.34 leukotriene-E4 20-monoxygenase
EC 1.14.13.35 anthranilate 3-monoxygenase (deaminating)
EC 1.14.13.36 5-O-(4-coumaroyl)-D-quinate 3′-monooxygenase
EC 1.14.13.37 methyltetrahydroprotoberberine 14-monoxygenase
EC 1.14.13.38 anhydrotetracycline monoxygenase
EC 1.14.13.39 nitric-oxide synthase
EC 1.14.13.40 anthraniloyl-CoA monoxygenase
EC 1.14.13.41 tyrosine N-monoxygenase
EC 1.14.13.42 hydroxyphenylacetonitrile 2-monoxygenase
EC 1.14.13.43 questin monoxygenase
EC 1.14.13.44 2-hydroxybiphenyl 3-monoxygenase
EC 1.14.13.45 now EC 1.14.18.2
EC 1.14.13.46 (+)-menthol monoxygenase
EC 1.14.13.47 (S)-limonene 3-monoxygenase
EC 1.14.13.48 (S)-limonene 6-monoxygenase
EC 1.14.13.49 (S)-limonene 7-monoxygenase
EC 1.14.13.50 pentachlorophenol monoxygenase
EC 1.14.13.51 6-oxocineole dehydrogenase
EC 1.14.13.52 isoflavone 3′-hydroxylase
EC 1.14.13.53 4′-methoxyisoflavone 2′-hydroxylase
EC 1.14.13.54 ketosteroid monoxygenase
EC 1.14.13.55 protopine 6-monoxygenase
EC 1.14.13.56 dihydroxysanguinarine 10-monoxygenase
EC 1.14.13.57 dihydrochelirubine 12-monoxygenase
EC 1.14.13.58 benzoyl-CoA 3-monoxygenase
EC 1.14.13.59 L-lysine 6-monoxygenase (NADPH)
EC 1.14.13.60 27-hydroxycholesterol 7α-monoxygenase
EC 1.14.13.61 2-hydroxyquinoline 8-monoxygenase
EC 1.14.13.62 4-hydroxyquinoline 3-monoxygenase
EC 1.14.13.63 3-hydroxyphenylacetate 6-hydroxylase
EC 1.14.13.64 4-hydroxybenzoate 1-hydroxylase
EC 1.14.13.65 deleted
EC 1.14.13.66 2-hydroxy-4-cyclohexanone 2-monoxygenase
EC 1.14.13.67 quinine 3-monoxygenase
EC 1.14.13.68 4-hydroxyphenylacetalddehyde oxime monoxygenase
EC 1.14.13.69 alkene monoxygenase
EC 1.14.13.70 sterol 14-demethylase
EC 1.14.13.71 N-methylcoclaurine 3′-monoxygenase
EC 1.14.13.72 methylsterol monooxygenase
EC 1.14.13.73 tabersonine 16-hydroxylase
EC 1.14.13.74 7-deoxyxylanin 7-hydroxylase
EC 1.14.13.75 vinoine hydroxylase
EC 1.14.13.76 taxane 10β-hydroxylase
EC 1.14.13.77 taxane 13α-hydroxylase
EC 1.14.13.78 ent-kaurane oxidase
EC 1.14.13.79 ent-kaurenoic acid oxidase
EC 1.14.13.80 (R)-limonene 6-monooxygenase
EC 1.14.13.81 magnesium-protoporphyrin IX monomethyl ester (oxidative) cyclase
EC 1.14.13.82 vanillate monooxygenase
EC 1.14.13.83 precorrin-3B synthase
EC 1.14.13.84 4-hydroxyacetoephone monooxygenase
EC 1.14.13.85 glycinechin synthase
EC 1.14.13.86 2-hydroxyisoflavone synthase
EC 1.14.13.87 licodione synthase
EC 1.14.13.88 flavonoid 3',5'-hydroxylase
EC 1.14.13.89 isoflavone 2'-hydroxylase
EC 1.14.13.90 zeaxanthin epoxidase
EC 1.14.13.91 deoxyspsarginine hydroxylase
EC 1.14.13.92 phenylacetone monooxygenase
EC 1.14.13.93 (+)-abscisic acid 8'-hydroxylase
EC 1.14.13.94 lithocholate 6β-hydroxylase
EC 1.14.13.95 7α-hydroxycholest-4-en-3-one 12α-hydroxylase
EC 1.14.13.96 5β-cholestan-3α,7α-diol 12α-hydroxylase
EC 1.14.13.97 taurchenodeoxycholate 6a-hydroxylase
EC 1.14.13.98 cholesterol 24-hydroxylase
EC 1.14.13.99 24-hydroxycholesterol 7α-hydroxylase
EC 1.14.13.100 25-hydroxycholesterol 7α-hydroxylase
EC 1.14.13.101 senecionine N-oxygenase

EC 1.14.14 With reduced flavin or flavoprotein as one donor, and incorporation of one atom of oxygen
EC 1.14.14.1 unspecific monooxygenase
EC 1.14.14.3 alkanal monooxygenase (FMN-linked)
EC 1.14.14.4 deleted, identical to EC 1.14.15.7
EC 1.14.14.5 alkanesulfonate monooxygenase

EC 1.14.15 With reduced iron-sulfur protein as one donor, and incorporation of one atom of oxygen
EC 1.14.15.1 camphor 5-monooxygenase
EC 1.14.15.2 camphor 1,2-monooxygenase
EC 1.14.15.3 alkane 1-monooxygenase
EC 1.14.15.4 steroid 11β-monooxygenase
EC 1.14.15.5 corticosterone 18-monooxygenase
EC 1.14.15.6 cholesterol monooxygenase (side-chain-cleaving)
EC 1.14.15.7 choline monooxygenase

EC 1.14.16 With reduced pteridine as one donor, and incorporation of one atom of oxygen
EC 1.14.16.1 phenylalanine 4-monooxygenase
EC 1.14.16.2 tyrosine 3-monooxygenase
EC 1.14.16.3 anthranilate 3-monooxygenase
EC 1.14.16.4 tryptophan 5-monooxygenase
EC 1.14.16.5 glycercyl-ether monooxygenase
EC 1.14.6 mandelate 4-monoxygenase

EC 1.14.17 With reduced ascorbate as one donor, and incorporation of one atom of oxygen
EC 1.14.17.1 dopamine β-monoxygenase
EC 1.14.17.2 deleted, included in EC 1.14.18.1
EC 1.14.17.3 peptidylglycine monoxygenase
EC 1.14.17.4 aminocyclopropane-carboxylate oxidase

EC 1.14.18 With another compound as one donor, and incorporation of one atom of oxygen
EC 1.14.18.1 monophenol monoxygenase
EC 1.14.18.2 CMP-N-acetylneuraminic monoxygenase

EC 1.14.19 With oxidation of a pair of donors resulting in the reduction of molecular oxygen to two molecules of water
EC 1.14.19.1 stearoyl-CoA 9-desaturase
EC 1.14.19.3 linoleoyl-CoA desaturase

EC 1.14.20 With 2-oxoglutarate as one donor, and the other dehydrogenated
EC 1.14.20.1 deacetoxycephalosporin-C synthase

EC 1.14.21 With NADH or NADPH as one donor, and the other dehydrogenated
EC 1.14.21.1 (S)-stypoline synthase
EC 1.14.21.2 (S)-cheilanthifoline synthase
EC 1.14.21.3 berbamine synthase
EC 1.14.21.4 salutaridine synthase
EC 1.14.21.5 (S)-canadine synthase
EC 1.14.21.6 lathosterol oxidase

EC 1.14.99 Miscellaneous
EC 1.14.99.1 prostaglandin-endoperoxide synthase
EC 1.14.99.2 kynurenine 7,8-hydroxylase
EC 1.14.99.3 heme oxygenase
EC 1.14.99.4 progesterone monoxygenase
EC 1.14.99.5 now EC 1.14.19.1
EC 1.14.99.7 squalene monoxygenase
EC 1.14.99.8 deleted, included in EC 1.14.1
EC 1.14.99.9 steroid 17α-monoxygenase
EC 1.14.99.10 steroid 21-monoxygenase
EC 1.14.99.11 estradiol 6β-monoxygenase
EC 1.14.99.12 4-androstene-3,17-dione monoxygenase
EC 1.14.99.14 progesterone 11α-monoxygenase
EC 1.14.99.15 4-methoxybenzoate monoxygenase (O-demethylating)
EC 1.14.99.16 now EC 1.14.13.72
EC 1.14.99.18 deleted
EC 1.14.99.19 plasmanyeathanolamine desaturase
EC 1.14.99.20 phyloquinone monoxygenase (2,3-epoxidizing)
EC 1.14.99.21 Lutia-luciferin monoxygenase (demethylating)
EC 1.14.99.22 ecdysone 20-monoxygenase
EC 1.14.99.23 3-hydroxybenzoate 2-monoxygenase
EC 1.14.99.24 steroid 9α-monoxygenase
EC 1.14.99.26 2-hydroxypyridine 5-monooxygenase  
EC 1.14.99.27 juglone 3-monooxygenase  
EC 1.14.99.28 linalool 8-monooxygenase  
EC 1.14.99.29 deoxyhypusine monooxygenase  
EC 1.14.99.30 carotene 7,8-desaturase  
EC 1.14.99.31 myristoyl-CoA 11-((E) desaturase  
EC 1.14.99.32 myristoyl-CoA 11-((Z) desaturase  
EC 1.14.99.33 δ12-fatty acid dehydrogenase  
EC 1.14.99.34 monoprenyl isoflavone epoxidase  
EC 1.14.99.35 thiophene-2-carboxyl-CoA monooxygenase  
EC 1.14.99.36 β-carotene 15,15'-monooxygenase  
EC 1.14.99.37 taxadiene 5α-hydroxylase  
EC 1.14.99.38 cholesterol 25-hydroxylase  

EC 1.15 Acting on superoxide as acceptor  
EC 1.15.1.1 superoxide dismutase  
EC 1.15.1.2 superoxide reductase  
EC 1.16 Oxidizing metal ions  

EC 1.16.1 With NAD+ or NADP+ as acceptor  
EC 1.16.1.1 mercury(II) reductase  
EC 1.16.1.2 diferric-transferrin reductase  
EC 1.16.1.3 aquacobalamin reductase  
EC 1.16.1.4 cob(II)alamin reductase  
EC 1.16.1.5 aquacobalamin reductase (NADPH)  
EC 1.16.1.6 cyanocobalamin reductase (cyanide-eliminating)  
EC 1.16.1.7 ferric-chelate reductase  
EC 1.16.1.8 [methionine synthase] reductase  

EC 1.16.3 With oxygen as acceptor  
EC 1.16.3.1 ferroxidase  
EC 1.16.8 With flavin as acceptor  
EC 1.16.8.1 cob(II)yrin acid a,c-diamide reductase  

EC 1.17 Acting on CH or CH2 groups  

EC 1.17.1 With NAD+ or NADP+ as acceptor  
EC 1.17.1.1 CDP-4-dehydro-6-deoxyglucose reductase  
EC 1.17.1.2 4-hydroxy-3-methylbut-2-enyl diphosphate reductase  
EC 1.17.1.3 leucoanthocyanidin reductase EC 1.17.1.4 xanthine dehydrogenase  
EC 1.17.1.5 nicotinate dehydrogenase  
EC 1.17.1.6 now EC 1.17.99.5  

EC 1.17.3 With oxygen as acceptor  
EC 1.17.3.1 pteridine oxidase  
EC 1.17.3.2 xanthine oxidase  
EC 1.17.3.3 6-hydroxynicotinate dehydrogenase  

EC 1.17.4 With a disulfide as acceptor  
EC 1.17.4.1 ribonucleoside-diphosphate reductase  
EC 1.17.4.2 ribonucleoside-triphosphate reductase  
EC 1.17.4.3 4-hydroxy-3-methylbut-2-en-1-yl diphosphate synthase  

EC 1.17.5 With a quinone or similar compound as acceptor  
EC 1.17.5.1 phenylacetyl-CoA dehydrogenase
EC 1.17.99 With other acceptors
EC 1.17.99.1 4-cresol dehydrogenase (hydroxylating)
EC 1.17.99.2 ethylbenzene hydroxylase
EC 1.17.99.3 3α,7α,12α-trihydroxy-5β-cholestanoyl-CoA 24-hydroxylase
EC 1.17.99.4 uracil/thymine dehydrogenase
EC 1.17.99.5 bile-acid 7α-dehydroxylase

EC 1.18 Acting on iron-sulfur proteins as donors

EC 1.18.1 With NAD\(^+\) or NADP\(^+\) as acceptor
EC 1.18.1.1 rubredoxin—NAD\(^+\) reductase
EC 1.18.1.2 ferredoxin—NADP\(^+\) reductase
EC 1.18.1.3 ferredoxin—NAD\(^+\) reductase
EC 1.18.1.4 rubredoxin—NAD(P)\(^+\) reductase

EC 1.18.3 With H\(^+\) as acceptor
EC 1.18.3.1 now EC 1.18.99.1

EC 1.18.6 With dinitrogen as acceptor
EC 1.18.6.1 nitrogenase

EC 1.18.96 With other, known, acceptors
EC 1.18.96.1 now EC 1.15.1.2

EC 1.18.99 With H\(^+\) as acceptors
EC 1.18.99.1 now EC 1.12.7.2
EC 1.19 Acting on reduced flavodoxin as donor

EC 1.19.6 With dinitrogen as acceptor
EC 1.19.6.1 nitrogenase (flavodoxin)
EC 1.20. Acting on phosphorus or arsenic in donors

EC 1.20.1 Acting on phosphorus or arsenic in donors, with NAD(P)\(^+\) as acceptor
EC 1.20.1.1 phosphonate dehydrogenase
EC 1.20.4 Acting on phosphorus or arsenic in donors, with disulfide as acceptor
EC 1.20.4.1 arsenate reductase (glutaredoxin)

EC 1.20.98 Acting on phosphorus or arsenic in donors, with other, known acceptors
EC 1.20.98.1 arsenate reductase (azurin)

EC 1.20.99 Acting on phosphorus or arsenic in donors, with other acceptors
EC 1.20.99.1 arsenate reductase (donor)

EC 1.21 Acting on X-H and Y-H to form an X-Y bond

EC 1.21.3 With oxygen as acceptor
EC 1.21.3.1 isopenicillin-N synthase
EC 1.21.3.2 columbamine oxidase
EC 1.21.3.3 reticuline oxidase
EC 1.21.3.4 sulochrin oxidase [(+)bisdechlorogodin-forming]
EC 1.21.3.5 sulochrin oxidase [(−)bisdechlorogodin-forming]
EC 1.21.3.6 aureusidin synthase

EC 1.21.4 With a disulfide as acceptor
EC 1.21.4.1 D-proline reductase (dithiol)
EC 1.21.4.2 glycine reductase
EC 1.21.4.3 sarcosine reductase
EC 1.21.4.4 betaine reductase
**EC 1.21.99 With other acceptors**
EC 1.21.99.1 β-cyclopiazonate dehydrogenase

EC 1.97 Other oxidoreductases
EC 1.97.1.1 chlorate reductase
EC 1.97.1.2 pyrogallol hydroxyltransferase
EC 1.97.1.3 sulfur reductase
EC 1.97.1.4 [formate-C-acetyltransferase]-activating enzyme
EC 1.97.1.5 now EC 1.20.4.1
EC 1.97.1.6 now EC 1.20.99.1
EC 1.97.1.7 now EC 1.20.4.2
EC 1.97.1.8 tetrachloroethene reductive dehalogenase
EC 1.97.1.9 selenate reductase
EC 1.97.1.10 thyroxine 5'-deiodinase
EC 1.97.1.11 thyroxine 5-deiodinase

**EC 2. Transferases**

**EC 2.1 Transferring One-Carbon Groups**

**EC 2.1.1 Methyltransferases**

EC 2.1.1.1 nicotinamide N-methyltransferase
EC 2.1.1.2 guanidinoacetate N-methyltransferase
EC 2.1.1.3 thieno—homocysteine S-methyltransferase
EC 2.1.1.4 acetylserotonin O-methyltransferase
EC 2.1.1.5 betaine—homocysteine S-methyltransferase
EC 2.1.1.6 catechol O-methyltransferase
EC 2.1.1.7 nicotine N-methyltransferase
EC 2.1.1.8 histamine N-methyltransferase
EC 2.1.1.9 thiol S-methyltransferase
EC 2.1.1.10 homocysteine S-methyltransferase
EC 2.1.1.11 magnesium protoporphyrin IX methyltransferase
EC 2.1.1.12 methionine S-methyltransferase
EC 2.1.1.13 methionine synthase
EC 2.1.1.14 S-methyltetrahydropteroylglutamate—homocysteine S-methyltransferase
EC 2.1.1.15 fatty-acid O-methyltransferase
EC 2.1.1.16 methylene-fatty-acyl-phospholipid synthase
EC 2.1.1.17 phosphatidylethanolamine N-methyltransferase
EC 2.1.1.18 polysaccharide O-methyltransferase
EC 2.1.1.19 trimethylsulfonium—tetrahydrofolate N-methyltransferase
EC 2.1.1.20 glycine N-methyltransferase
EC 2.1.1.21 methylvamine—glutamate N-methyltransferase
EC 2.1.1.22 carnosine N-methyltransferase
EC 2.1.1.23 now covered by EC 2.1.1.124, EC 2.1.1.125 and EC 2.1.1.126
EC 2.1.1.24 now covered by EC 2.1.1.77, EC 2.1.1.80 and EC 2.1.1.100
EC 2.1.1.25 phenol O-methyltransferase
EC 2.1.1.26 iodophenol O-methyltransferase
EC 2.1.1.27 tyramine N-methyltransferase
EC 2.1.1.28 phenylethanolamine N-methyltransferase
EC 2.1.1.29 tRNA (cytosine-5')-methyltransferase
EC 2.1.1.30 deleted
EC 2.1.1.31 tRNA (guanine-N^4)-methyltransferase
EC 2.1.1.32 tRNA (guanine-N^2)-methyltransferase
EC 2.1.1.33 tRNA (guanine-N^3)-methyltransferase
EC 2.1.1.34 tRNA (guanosine-2'-O)-methyltransferase
EC 2.1.1.35 tRNA (uracil-5')-methyltransferase
EC 2.1.1.36 tRNA (adenine-N^6)-methyltransferase
EC 2.1.1.37 DNA (cytosine-5')-methyltransferase
EC 2.1.1.38 O-demethylpuromycin O-methyltransferase
EC 2.1.1.39 inositol 3-methyltransferase
EC 2.1.1.40 inositol 1-methyltransferase
EC 2.1.1.41 sterol 24-C-methyltransferase
EC 2.1.1.42 luteolin O-methyltransferase
EC 2.1.1.43 histone-lysine N-methyltransferase
EC 2.1.1.44 dimethylhistidine N-methyltransferase
EC 2.1.1.45 thymidylate synthase
EC 2.1.1.46 isoflavone 4'-O-methyltransferase
EC 2.1.1.47 indolepyruvate C-methyltransferase
EC 2.1.1.48 rRNA (adenine-N^6)-methyltransferase
EC 2.1.1.49 amine N-methyltransferase
EC 2.1.1.50 loganate O-methyltransferase
EC 2.1.1.51 tRNA (guanine-N^3)-methyltransferase
EC 2.1.1.52 tRNA (guanine-N^2)-methyltransferase
EC 2.1.1.53 putrescine N-methyltransferase
EC 2.1.1.54 deoxyctydylate C-methyltransferase
EC 2.1.1.55 tRNA (adenine-N^6)-methyltransferase
EC 2.1.1.56 mRNA (guanine-N^3)-methyltransferase
EC 2.1.1.57 mRNA (nucleoside-2'-O)-methyltransferase
EC 2.1.1.58 deleted, included in EC 2.1.1.57
EC 2.1.1.59 [cytochrome c]-lysine N-methyltransferase
EC 2.1.1.60 calmodulin-lysine N-methyltransferase
EC 2.1.1.61 tRNA (5-methylaminomethyl-2-thioridylate)-methyltransferase
EC 2.1.1.62 mRNA (2'-O-methyladenosine-N^6)-methyltransferase
EC 2.1.1.63 methylated-DNA—[protein]-cysteine S-methyltransferase
EC 2.1.1.64 3-demethylubiquinone-9 3-O-methyltransferase
EC 2.1.1.65 lycopodine 2'-O-methyltransferase
EC 2.1.1.66 rRNA (adenosine-2'-O)-methyltransferase
EC 2.1.1.67 thiopurine S-methyltransferase
EC 2.1.1.68 caffeate O-methyltransferase
EC 2.1.1.69 5-hydroxyfuranocoumarin 5-O-methyltransferase
EC 2.1.1.70 8-hydroxyfuranocoumarin 8-O-methyltransferase
EC 2.1.1.71 phosphatidyl-N-methylolamidine N-methyltransferase
EC 2.1.1.72 site-specific DNA-methyltransferase (adenine-specific)
EC 2.1.1.73 deleted
EC 2.1.1.74 methylenetetrahydrofolate—tRNA-(uracil-5')-methyltransferase (FADH_2-oxidizing)
EC 2.1.1.75 apigenin 4'-O-methyltransferase
EC 2.1.1.76 quercetin 3-O-methyltransferase
EC 2.1.1.77 protein-L-isosapramide(D-aspartate) O-methyltransferase
EC 2.1.1.78 isoorientin 3'-O-methyltransferase
EC 2.1.1.79 cyclopropane-fatty-acyl-phospholipid synthase
EC 2.1.1.80 protein-glutamate O-methyltransferase
EC 2.1.1.81 deleted, included in EC 2.1.1.49
EC 2.1.1.82 3-methylquercetin 7-O-methyltransferase
EC 2.1.1.83 3,7-dimethylquercetin 4'-O-methyltransferase
EC 2.1.1.84 methylquercetin 6-O-methyltransferase
EC 2.1.1.85 protein-histidine N-methyltransferase
EC 2.1.1.86 tetrahydromethanopterin S-methyltransferase
EC 2.1.1.87 pyridine N-methyltransferase
EC 2.1.1.88 8-hydroxyquercetin 8-O-methyltransferase
EC 2.1.1.89 tetrahydrocolumbamine 2-O-methyltransferase
EC 2.1.1.90 methanol—5-hydroxybenzimidazolylcobamide Co-methyltransferase
EC 2.1.1.91 isobutyraldoxime O-methyltransferase
EC 2.1.1.92 bergaptol O-methyltransferase
EC 2.1.1.92 deleted, now EC 2.1.1.69
EC 2.1.1.93 xanthotoxol O-methyltransferase
EC 2.1.1.94 11-O-demethyl-17-0-deacetylvinodoline O-methyltransferase
EC 2.1.1.95 tocopherol O-methyltransferase
EC 2.1.1.96 thioether S-methyltransferase
EC 2.1.1.97 3-hydroxyxanthanilate 4-C-methyltransferase
EC 2.1.1.98 diphtrine synthase
EC 2.1.1.99 16-methoxy-2,3-dihydro-3-hydroxytabersonine N-methyltransferase
EC 2.1.1.100 protein-S-isoprenylcysteine O-methyltransferase
EC 2.1.1.101 macrocin O-methyltransferase
EC 2.1.1.102 demethylmacrocin O-methyltransferase
EC 2.1.1.103 phosphochanolamine N-methyltransferase
EC 2.1.1.104 caffeoyl-CoA O-methyltransferase
EC 2.1.1.105 N-benzoyl-4-hydroxyxanthanilate 4-O-methyltransferase
EC 2.1.1.106 tryptophan 2-C-methyltransferase
EC 2.1.1.107 uroporphyrinogen-III C-methyltransferase
EC 2.1.1.108 6-hydroxymellein O-methyltransferase
EC 2.1.1.109 demethylsterigmatocystin 6-O-methyltransferase
EC 2.1.1.110 sterigmatocystin 7-O-methyltransferase
EC 2.1.1.111 anthranilate N-methyltransferase
EC 2.1.1.112 glucuronoxylan 4-O-methyltransferase
EC 2.1.1.113 site-specific DNA-methyltransferase (cytosine-N⁶-specific)
EC 2.1.1.114 hexaprenyldihydroxybenzoate methyltransferase
EC 2.1.1.115 (RS)-1-benzyl-1,2,3,4-tetrahydroisoquinoline N-methyltransferase
EC 2.1.1.116 3'-hydroxy-N-methyl-(S)-coclaurine 4'-O-methyltransferase
EC 2.1.1.117 (S)-scoulerine 9-O-methyltransferase
EC 2.1.1.118 columbamine N-methyltransferase
EC 2.1.1.119 10-hydroxydihydrosanguinarine 10-O-methyltransferase
EC 2.1.1.120 12-hydroxydihydrochelirubine 12-O-methyltransferase
EC 2.1.1.121 6-O-methylinorlaudanosoline 5'-O-methyltransferase
EC 2.1.1.122 (S)-tetrahydroprotoberberine N-methyltransferase
EC 2.1.1.123 [cytochrome c]-methionine S-methyltransferase
EC 2.1.1.124 [cytochrome c]-arginine N-methyltransferase
EC 2.1.1.125 histone-arginine N-methyltransferase
EC 2.1.1.126 [myelin basic protein]-arginine N-methyltransferase
EC 2.1.1.127 [ribulose-bisphosphate carboxylase]-lysine N-methyltransferase
EC 2.1.1.128 (RS)-norcoclaurine 6-O-methyltransferase
EC 2.1.1.129 mositol 4-methyltransferase
EC 2.1.1.130 precorrin-2 C⁰⁰-methyltransferase
EC 2.1.1.131 precorrin-3B C²⁰-methyltransferase
EC 2.1.1.132 precorrin-6Y C₁⁰₅-methyltransferase (decarboxylating)
EC 2.1.1.133 precorrin-4 C¹⁴-methyltransferase
EC 2.1.1.134 now with EC 2.1.1.129
EC 2.1.1.135 now EC 1.16.1.8
EC 2.1.1.136 chlorophenol O-methyltransferase
EC 2.1.1.137 arsename methyltransferase
EC 2.1.1.138 deleted
EC 2.1.1.139 3'-demethylstaurosporine O-methyltransferase
EC 2.1.1.140 (S)-coclaurine-N-methyltransferase
EC 2.1.1.141 jasmonate O-methyltransferase
EC 2.1.1.142 cycloartenol 24-C-methyltransferase
EC 2.1.1.143 24-methylene-sterol C-methyltransferase
EC 2.1.1.144 trans-aconitate 2-methyltransferase
EC 2.1.1.145 trans-aconitate 3-methyltransferase
EC 2.1.1.146 (iso)eugenol O-methyltransferase
EC 2.1.1.147 corydaline synthase
EC 2.1.1.148 thymidylate synthase (FAD)
EC 2.1.1.149 myricetin O-methyltransferase
EC 2.1.1.150 isoflavone 7-O-methyltransferase
EC 2.1.1.151 cobalt-factor II C^20^-methyltransferase
EC 2.1.1.152 precorrin-6A synthase (deacetylating)
EC 2.1.1.153 vitexin 2''-O-rhamnoside 7-O-methyltransferase
EC 2.1.1.154 isoliquiritinigen 2''-O-methyltransferase
EC 2.1.1.155 kaempferol 4''-O-methyltransferase
EC 2.1.1.156 glycine/sarcosine N-methyltransferase
EC 2.1.1.157 sarcosine/dimethylglycine N-methyltransferase

EC 2.1.2 Hydroxymethyl-, Formyl- and Related Transferases

EC 2.1.2.1 glycine hydroxymethyltransferase
EC 2.1.2.2 phosphoribosylglycinamide formyltransferase
EC 2.1.2.3 phosphoribosylaminomimidazolecarboxamide formyltransferase
EC 2.1.2.4 glycine formiminotransferase
EC 2.1.2.5 glutamate formiminotransferase
EC 2.1.2.6 deleted, included in EC 2.1.2.5
EC 2.1.2.7 D-alanine 2-hydroxymethyltransferase
EC 2.1.2.8 deoxycytidylate 5-hydroxymethyltransferase
EC 2.1.2.9 methionyl-tRNA formyltransferase
EC 2.1.2.10 aminomethyltransferase
EC 2.1.2.11 3-methyl-2-oxobutanoate hydroxymethyltransferase
EC 2.1.2.12 now EC 2.1.1.74

EC 2.1.3 Carboxy- and Carbamoyltransferases

EC 2.1.3.1 methylmalonyl-CoA carboxytransferase
EC 2.1.3.2 aspartate carbamoyltransferase
EC 2.1.3.3 ornithine carbamoyltransferase
EC 2.1.3.4 deleted
EC 2.1.3.5 oxamate carbamoyltransferase
EC 2.1.3.6 putrescine carbamoyltransferase
EC 2.1.3.7 3-hydroxymethylisocroman carboxamoyltransferase
EC 2.1.3.8 lysine carbamoyltransferase
EC 2.1.3.9 N-acetylcysteine carbamoyltransferase

EC 2.1.4 Amidinotransferases

EC 2.1.4.1 glycine amidinotransferase
EC 2.1.4.2 scyllo-inosamine-4-phosphate amidinotransferase
EC 2.2 Transferring Aldehyde or Ketonic Groups

EC 2.2.1 Transketolases and Transaldolases

EC 2.2.1.1 transketolase
EC 2.2.1.2 transaldolase
EC 2.2.1.3 formaldehyde transketolase
EC 2.2.1.4 acetoin—ribose-5-phosphate transaldolase
EC 2.2.1.5 2-hydroxy-3-oxoadipate synthase
EC 2.2.1.6 acetalactate synthase
EC 2.2.1.7 1-deoxy-D-xylulose-5-phosphate synthase
EC 2.2.1.8 fluorothronine transaldolase

EC 2.3 Acyltransferases

EC 2.3.1 Transferring groups other than amino-acyl groups

EC 2.3.1.1 amino-acid N-acetyltansferase
EC 2.3.1.2 imidazole N-acetyltansferase
EC 2.3.1.3 glucosamine N-acetyltransferase
EC 2.3.1.4 glucosamine-phosphate N-acetyltransferase
EC 2.3.1.5 arylamine N-acetyltransferase
EC 2.3.1.6 choline O-acetyltransferase
EC 2.3.1.7 carnitine O-acetyltransferase
EC 2.3.1.8 phosphate acetyltransferase
EC 2.3.1.9 acetyl-CoA C-acetyltransferase
EC 2.3.1.10 hydrogen-sulfide S-acetyltransferase
EC 2.3.1.11 thioethanolamine S-acetyltransferase
EC 2.3.1.12 dihydrolipooyllysine-residue acetyltransferase
EC 2.3.1.13 glycine N-acetyltransferase
EC 2.3.1.14 glutamine N-phenylacetlytransferase
EC 2.3.1.15 glycerol-3-phosphate O-acetyltransferase
EC 2.3.1.16 acetyl-CoA C-acetyltransferase
EC 2.3.1.17 aspartate N-acetyltransferase
EC 2.3.1.18 galactoside O-acetyltransferase
EC 2.3.1.19 phosphate butyryltransferase
EC 2.3.1.20 diacylglycerol O-acetyltransferase
EC 2.3.1.21 carnitine O-palmitoyltransferase
EC 2.3.1.22 2-acylglycerol O-acetyltransferase
EC 2.3.1.23 1-acylglycerophosphocholine O-acetyltransferase
EC 2.3.1.24 sphingosine N-acetyltransferase
EC 2.3.1.25 plasmalogen synthase
EC 2.3.1.26 sterol O-acetyltransferase
EC 2.3.1.27 cortisol O-acetyltransferase
EC 2.3.1.28 chloramphemicol O-acetyltransferase
EC 2.3.1.29 glycine C-acetyltransferase
EC 2.3.1.30 serine O-acetyltransferase
EC 2.3.1.31 homoscrine O-acetyltransferase
EC 2.3.1.32 lysine N-acetyltransferase
EC 2.3.1.33 histidine N-acetyltransferase
EC 2.3.1.34 D-tryptophan N-acetyltransferase
EC 2.3.1.35 glutamate N-acetyltransferase
EC 2.3.1.36 D-amino-acid N-acetyltransferase
EC 2.3.1.37 5-aminolevulinate synthase
EC 2.3.1.38 [acyl-carrier-protein] S-acetyltransferase
EC 2.3.1.39 [acyl-carrier-protein] S-malonyltransferase
EC 2.3.1.40 acyl-[acyl-carrier-protein]—phospholipid O-acyltransferase
EC 2.3.1.41 β-ketoacyl-acyl-carrier-protein synthase I
EC 2.3.1.42 glycerol-3-phosphate O-acyltransferase
EC 2.3.1.43 phosphatidylcholine—sterol O-acyltransferase
EC 2.3.1.44 N-acetylneuraminate 4-O-acyltransferase
EC 2.3.1.45 N-acetylneuraminate 7-O(or 9-O)-acyltransferase
EC 2.3.1.46 homoserine O-succinyltransferase
EC 2.3.1.47 8-amino-7-oxononanoate synthase
EC 2.3.1.48 histone acetyltransferase
EC 2.3.1.49 deacetyl-[citrate-(pro-3S)]-lyase] S-acetyltransferase
EC 2.3.1.50 serine C-palmitoyltransferase
EC 2.3.1.51 1-acylglycerol-3-phosphate O-acyltransferase
EC 2.3.1.52 2-acylglycerol-3-phosphate O-acyltransferase
EC 2.3.1.53 phenylalanine N-acyltransferase
EC 2.3.1.54 formate C-acetyltransferase
EC 2.3.1.55 now EC 2.3.1.82
EC 2.3.1.56 aromatic-hydroxylamine O-acetyltransferase
EC 2.3.1.57 diamine N-acetyltransferase
EC 2.3.1.58 2,3-diaminopropionate N-oxalyltransferase
EC 2.3.1.59 gentamicin 2'-N-acetyltransferase
EC 2.3.1.60 gentamicin 3'-N-acetyltransferase
EC 2.3.1.61 dihydrofolylpolyamine-residue succinyltransferase
EC 2.3.1.62 2-acylglycerophosphocholine O-acyltransferase
EC 2.3.1.63 1-alkylglycerocephosphocholine O-acyltransferase
EC 2.3.1.64 agmatine N^1-coumaroyltransferase
EC 2.3.1.65 bile acid-CoA:amino acid N-acyltransferase
EC 2.3.1.66 leucine N-acetyltransferase
EC 2.3.1.67 1-alkylglycerophosphocholine O-acyltransferase
EC 2.3.1.68 glutamine N-acetyltransferase
EC 2.3.1.69 monoterpenol O-acetyltransferase
EC 2.3.1.70 CDP-acylglycerol O-arachidonoyltransferase
EC 2.3.1.71 glycine N-benzoyltransferase
EC 2.3.1.72 indolacetylglucose—inositol O-acyltransferase
EC 2.3.1.73 diacylglycerol—sterol O-acyltransferase
EC 2.3.1.74 naringenin-chalcone synthase
EC 2.3.1.75 long-chain-alcohol O-fatty-acyltransferase
EC 2.3.1.76 retinol O-fatty-acyltransferase
EC 2.3.1.77 triacylglycerol—sterol O-acyltransferase
EC 2.3.1.78 heparan-α-glucosaminide N-acetyltransferase
EC 2.3.1.79 maltose O-acetyltransferase
EC 2.3.1.80 cysteine-S-conjugate N-acetyltransferase
EC 2.3.1.81 aminoglycoside N^2-acyltransferase
EC 2.3.1.82 aminoglycoside N^4-acyltransferase
EC 2.3.1.83 phosphatidylcholine—dolichol O-acyltransferase
EC 2.3.1.84 alcohol O-acetyltransferase
EC 2.3.1.85 fatty-acid synthase
EC 2.3.1.86 fatty-acyl-CoA synthase
EC 2.3.1.87 aralkylamine N-acetyltransferase
EC 2.3.1.88 peptide α-N-acetyltransferase
EC 2.3.1.89 tetraphydriodipicolinate N-acetyltransferase
EC 2.3.1.90 β-glucogallin O-galloyltransferase
EC 2.3.1.91 sinapoylgucose—choline O-sinapoyltransferase
EC 2.3.1.92 sinapoylgucose—malate O-sinapoyltransferase
EC 2.3.1.93 13-hydroxylupinine O-tigloyltransferase
EC 2.3.1.94 erythronolide synthase
EC 2.3.1.95 trihydroxystilbene synthase
EC 2.3.1.96 glycoprotein N-palmitoyltransferase
EC 2.3.1.97 glycylpeptide N-tetradecanoyltransferase
EC 2.3.1.98 chlorogenate—glucarate O-hydroxycinnamoyltransferase
EC 2.3.1.99 quinate O-hydroxycinnamoyltransferase
EC 2.3.1.100 [myelin-prototripotid] O-palmitoyltransferase
EC 2.3.1.101 formylmethanofuran—tetrahydromethanopterin N-formyltransferase
EC 2.3.1.102 N'-hydroxylysine O-acetyltransferase
EC 2.3.1.103 sinapoylgucose—sinapoylgucose O-sinapoyltransferase
EC 2.3.1.104 1-alkenylglycerolglycerophosphate O-acetyltransferase
EC 2.3.1.105 alkylglycerolphosphate 2-O-acetyltransferase
EC 2.3.1.106 tartronate O-hydroxycinnamoyltransferase
EC 2.3.1.107 17-O-deacetylvindoline O-acetyltransferase
EC 2.3.1.108 α-tubulin N-acetyltransferase
EC 2.3.1.109 arginine N-succinyltransferase
EC 2.3.1.110 tyramine N-feruloyltransferase
EC 2.3.1.111 mycocerosate synthase
EC 2.3.1.112 D-tryptophan N-malonyltransferase
EC 2.3.1.113 anthranilate N-malonyltransferase
EC 2.3.1.114 3,4-dichloroaniline N-malonyltransferase
EC 2.3.1.115 isoflavone-7-O-β-glucoside 6''-O-malonyltransferase
EC 2.3.1.116 flavonol-3-O-β-glucoside O-malonyltransferase
EC 2.3.1.117 2,3,4,5-tetrahdropyridine-2,6-dicarboxylate N-succinyltransferase
EC 2.3.1.118 N-hydroxycinnamoylamine O-acetyltransferase
EC 2.3.1.119 icosanoyl-CoA synthase
EC 2.3.1.120 deleted
EC 2.3.1.121 1-alkenylglycerolphosphoethanolamine O-acetyltransferase
EC 2.3.1.122 trehalose O-mycocolyltransferase
EC 2.3.1.123 dolichol O-acetyltransferase
EC 2.3.1.124 deleted
EC 2.3.1.125 1-alkyl-2-acetylglycerol O-acetyltransferase
EC 2.3.1.126 isocitrate O-dihydroxycinnamoyltransferase
EC 2.3.1.127 ornithine N-benzoyltransferase
EC 2.3.1.128 ribosomal-protein-alanine N-acetyltransferase
EC 2.3.1.129 acyl-[acyl-carrier-protein]—UDP-N-acetylglycosamine O-acetyltransferase
EC 2.3.1.130 galactarate O-hydroxycinnamoyltransferase
EC 2.3.1.131 glucarate O-hydroxycinnamoyltransferase
EC 2.3.1.132 glucarolactone O-hydroxycinnamoyltransferase
EC 2.3.1.133 shikimate O-hydroxycinnamoyltransferase
EC 2.3.1.134 galactolipid O-acetyltransferase
EC 2.3.1.135 phosphatidycholine—retinol O-acetyltransferase
EC 2.3.1.136 polysialic-acid O-acetyltransferase
EC 2.3.1.137 carnitine O-octanoyltransferase
EC 2.3.1.138 putrescine N-hydroxycinnamoyltransferase
EC 2.3.1.139 ecdysone O-acetyltransferase
EC 2.3.1.140 rosmarinate synthase
EC 2.3.1.141 galactosylacylglycerol O-acetyltransferase
EC 2.3.1.142 glycoprotein O-fatty-acetyltransferase
EC 2.3.1.143 β-glucogallin—tetrakisgalloylgucose O-galloyltransferase
EC 2.3.1.144 anthranilate N-benzoyltransferase
EC 2.3.1.145 piperidine N-piperoyltransferase
EC 2.3.1.146 pinosylvin synthase
EC 2.3.1.147 glycerophospholipid arachidonoyl-transferase (CoA-independent)
EC 2.3.1.148 glycerophospholipid acyltransferase (CoA-dependent)
EC 2.3.1.149 platelet-activating factor acetyltransferase
EC 2.3.1.150 salutaridinol 7-O-acetyltransferase
EC 2.3.1.151 benzophenone synthase
EC 2.3.1.152 alcohol O-cinnamoyltransferase
EC 2.3.1.153 anthocyanin 5-aromatic acyltransferase
EC 2.3.1.154 propionyl-CoA C13-trimethyltridecanoyltransferase
EC 2.3.1.155 acetyl-CoA C-myristoyltransferase
EC 2.3.1.156 phloroisovalerophenone synthase
EC 2.3.1.157 glucosamine-1-phosphate N-acetyltransferase
EC 2.3.1.158 phospholipid:diacetyl glycerol acyltransferase
EC 2.3.1.159 acridone synthase
EC 2.3.1.160 vinorine synthase
EC 2.3.1.161 lovastatin nonaketide synthase
EC 2.3.1.162 taxadien-5α-ol O-acetyltransferase
EC 2.3.1.163 10-hydroxytaxane O-acetyltransferase
EC 2.3.1.164 isopenicillin-N-N-acetyltransferase
EC 2.3.1.165 6-methylsalicylic acid synthase
EC 2.3.1.166 2α-hydroxytaxane 2-O-benzylotransferase
EC 2.3.1.167 10-deacetylbaccatin III 10-O-acetyltransferase
EC 2.3.1.168 dihydroxyphenyllysine-residue (2-methylpropanoyl)transferase
EC 2.3.1.169 CO-methylating acetyl-CoA synthase
EC 2.3.1.170 6′-deoxychalcone synthase
EC 2.3.1.171 anthocyanin 6′-O-malonyltransferase
EC 2.3.1.172 anthocyanin 5-O-glucoside 6′-O-malonyltransferase
EC 2.3.1.173 flavonol-3-O-triglucoside O-coumaroyltransferase EC 2.3.1.174 3-oxoadipyl-CoA thiolase
EC 2.3.1.175 deacetylcephalosporin-C acetyltransferase
EC 2.3.1.176 propanoyl-CoA C-acyltransferase
EC 2.3.1.177 biphenyl synthase
EC 2.3.1.178 diaminobutyrate acetyltransferase
EC 2.3.1.179 β-ketoacyl-acyl-carrier-protein synthase II
EC 2.3.1.180 β-ketoacyl-acyl-carrier-protein synthase III
EC 2.3.1.181 lipoxy(ocanoyl) transferase

EC 2.3.2 Aminoacyltransferases

EC 2.3.2.1 D-glutamyltransferase
EC 2.3.2.2 γ-glutamyltransferase
EC 2.3.2.3 lysyltransferase
EC 2.3.2.4 γ-glutamylcyclotransferase
EC 2.3.2.5 glutaminyl-peptide cyclotransferase
EC 2.3.2.6 leucyltransferase
EC 2.3.2.7 aspartyltransferase
EC 2.3.2.8 arginyltransferase
EC 2.3.2.9 agaritine γ-glutamyltransferase
EC 2.3.2.10 UDP-N-acetylglucosaminepentapeptide-lysine Nε-alanyltransferase
EC 2.3.2.11 alanophosphatidylglycerol synthase
EC 2.3.2.12 peptidyltransferase
EC 2.3.2.13 protein-glutamine γ-glutamyltransferase
EC 2.3.2.14 D-alanine γ-glutamyltransferase
EC 2.3.2.15 glutathione γ-glutamylcysteinyltransferase

EC 2.3.3 Acyl groups converted into alkyl on transfer
EC 2.3.3.1 citrate (Si)-synthase
EC 2.3.3.2 decylcitrate synthase
EC 2.3.3.3 citrate (Ro)-synthase
EC 2.3.3.4 decylhomocitrate synthase
EC 2.3.3.5 2-methylcitrate synthase
EC 2.3.3.6 2-ethylmalate synthase
EC 2.3.3.7 3-ethylmalate synthase
EC 2.3.3.8 ATP citrate synthase
EC 2.3.3.9 malate synthase
EC 2.3.3.10 hydroxymethylglutaryl-CoA synthase
EC 2.3.3.11 2-hydroxyglutarate synthase
EC 2.3.3.12 3-propylmalate synthase
EC 2.3.3.13 2-isopropylmalate synthase
EC 2.3.3.14 homocitrate synthase
EC 2.3.3.15 sulfoacetalddehyde acetyltransferase

EC 2.4 Glycosyltransferases

EC 2.4.1.1 phosphorylase
EC 2.4.1.2 dextrin dextranase
EC 2.4.1.3 deleted, included in EC 2.4.1.25
EC 2.4.1.4 amylosucrase
EC 2.4.1.5 dextranucrase
EC 2.4.1.6 deleted
EC 2.4.1.7 sucrose phosphorylase
EC 2.4.1.8 maltose phosphorylase
EC 2.4.1.9 inulosucrase
EC 2.4.1.10 levansucrase
EC 2.4.1.11 glycogen(starch) synthase
EC 2.4.1.12 cellulose synthase (UDP-forming)
EC 2.4.1.13 sucrose synthase
EC 2.4.1.14 sucrose-phosphate synthase
EC 2.4.1.15 α,α-trehalose-phosphate synthase (UDP-forming)
EC 2.4.1.16 chitin synthase
EC 2.4.1.17 glucuronosyltransferase
EC 2.4.1.18 1,4-α-glucan branching enzyme
EC 2.4.1.19 cyclomaltoolternate gluconotransferase
EC 2.4.1.20 cellulbiose phosphorylase
EC 2.4.1.21 starch synthase
EC 2.4.1.22 lactose synthase
EC 2.4.1.23 sphingosine β-galactosyltransferase
EC 2.4.1.24 1,4-α-glucan 6-α-glucosyltransferase
EC 2.4.1.25 4-α-glucanotransferase
EC 2.4.1.26 DNA α-glucosyltransferase
EC 2.4.1.27 DNA β-glucosyltransferase
EC 2.4.1.28 glucosyl-DNA β-glucosyltransferase
EC 2.4.1.29 cellulose synthase (GDP-forming)
EC 2.4.1.30 1,3-β-oligoglucan phosphorylase
EC 2.4.1.31 laminaribiose phosphorylase
EC 2.4.1.32 glucomannan 4-β-mannosyltransferase
EC 2.4.1.33 alginate synthase
EC 2.4.1.34 1,3-β-glucan synthase
EC 2.4.1.35 phenol β-glucosyltransferase
EC 2.4.1.36 α,α-trehalose-phosphate synthase (GDP-forming)
EC 2.4.1.37 fucosylgalactoside 3-α-galactosyltransferase
EC 2.4.1.38 β-N-acetylglucosaminyl-glycopeptide β-1,4-galactosyltransferase
EC 2.4.1.39 steroid N-acetylglucosaminyltransferase
EC 2.4.1.40 glycoprotein-fucosylgalactoside α-N-acetylgalactosaminyltransferase
EC 2.4.1.41 galactoside α-N-acetylgalactosaminyltransferase
EC 2.4.1.42 deleted, included in EC 2.4.1.17
EC 2.4.1.43 polygalacturonate 4-α-galacturonosyltransferase
EC 2.4.1.44 lipopolysaccharide 3-α-galactosyltransferase
EC 2.4.1.45 2-hydroxyacylsphingosine 1-β-galactosyltransferase
EC 2.4.1.46 monogalactosyldiacylglycerol synthase
EC 2.4.1.47 N-acethylphosphosine galactosyltransferase
EC 2.4.1.48 heteroglycan α-mannosyltransferase
EC 2.4.1.49 cellobextrin phosphorylase
EC 2.4.1.50 procollagen galactosyltransferase
EC 2.4.1.51 now covered by EC 2.4.1.101, EC 2.4.1.143, EC 2.4.1.144 and EC 2.4.1.145
EC 2.4.1.52 poly(glycerol-phosphate) α-galactosyltransferase
EC 2.4.1.53 poly(ribitol-phosphate) β-galactosyltransferase
EC 2.4.1.54 undecaprenyl-phosphate mannosyltransferase
EC 2.4.1.55 now EC 2.7.8.14
EC 2.4.1.56 lipopolysaccharide N-acetylgalactosaminyltransferase
EC 2.4.1.57 phosphatidylinositol α-mannosyltransferase
EC 2.4.1.58 lipopolysaccharide glucosyltransferase I
EC 2.4.1.59 deleted, included in EC 2.4.1.17
EC 2.4.1.60 abequosyltransferase
EC 2.4.1.61 deleted, included in EC 2.4.1.17
EC 2.4.1.62 ganglioside galactosyltransferase
EC 2.4.1.63 linamar synthase
EC 2.4.1.64 α,α-trehalose phosphorylase
EC 2.4.1.65 3-galactosyl-N-acetylgalcosaminide 4-α-L-fucosyltransferase
EC 2.4.1.66 procollagen galactosyltransferase
EC 2.4.1.67 galactosin—raffinose galactosyltransferase
EC 2.4.1.68 glycoprotein 6-α-L-fucosyltransferase
EC 2.4.1.69 galactoside 2-α-L-fucosyltransferase
EC 2.4.1.70 poly(ribitol-phosphate) N-acetylgalactosaminyl-transferase
EC 2.4.1.71 aryamine glucosyltransferase
EC 2.4.1.72 now EC 2.4.2.24
EC 2.4.1.73 lipopolysaccharide glucosyltransferase II
EC 2.4.1.74 glycosaminoglycan galactosyltransferase
EC 2.4.1.75 deleted entry
EC 2.4.1.76 deleted, included in EC 2.4.1.17
EC 2.4.1.77 deleted, included in EC 2.4.1.17
EC 2.4.1.78 phosphopolyprenol glucosyltransferase
EC 2.4.1.79 globotriaosylceramide 3-β-N-acetylgalactosaminyltransferase
EC 2.4.1.80 ceramide glucosyltransferase
EC 2.4.1.81 flavone 7-O-β-glucosyltransferase
EC 2.4.1.82 galactosin—sucrose galactosyltransferase
EC 2.4.1.83 dolichyl-phosphate β-D-mannosyltransferase
EC 2.4.1.84 deleted, included in EC 2.4.1.17
EC 2.4.1.85 cyanohydrin β-glucosyltransferase
EC 2.4.1.86 glucosaminylgalactosylglucosylceramide β-galactosyltransferase
EC 2.4.1.87 N-acetylactosaminide 3-α-galactosyltransferase
EC 2.4.1.88 globoside α-N-acetylgalactosaminyltransferase
EC 2.4.1.89 deleted, included in EC 2.4.1.69
EC 2.4.1.90 N-acetyllactosamine synthase
EC 2.4.1.91 flavonol 3-O-glucosyltransferase
EC 2.4.1.92 (N-acetylneuraminyl)-galactosylglucosylceramide N-acetylgalactosaminyltransferase
EC 2.4.1.93 now EC 4.2.2.18
EC 2.4.1.94 protein N-acetylglucosaminyltransferase
EC 2.4.1.95 bilirubin-glucuronoside glucuronosyltransferase
EC 2.4.1.96 sn-glycerol-3-phosphate 1-galactosyltransferase
EC 2.4.1.97 1,3-β-D-glucan phosphorylase
EC 2.4.1.98 deleted, included in EC 2.4.1.90
*EC 2.4.1.99 sucrose:sucrose fructosyltransferase
*EC 2.4.1.100 2,1-fructan:2,1-fructan 1-fructosyltransferase
EC 2.4.1.101 α-1,3-mannosyl-glycoprotein 2-β-N-acetylglucosaminyltransferase
EC 2.4.1.102 β-1,3-galactosyl-O-glycosyl-glycoprotein β-1,6-N-acetylglucosaminyltransferase
EC 2.4.1.103 alizarin 2-β-glucosyltransferase
EC 2.4.1.104 α-dihydroxycoumarin 7-O-glucosyltransferase
EC 2.4.1.105 vitexin β-glucosyltransferase
EC 2.4.1.106 isovitexin β-glucosyltransferase
EC 2.4.1.107 deleted, included in EC 2.4.1.17
EC 2.4.1.108 deleted, included in EC 2.4.1.17
EC 2.4.1.109 dolichyl-phosphate-mannose-protein mannosyltransferase
EC 2.4.1.110 tRNA-queuosine β-mannosyltransferase
EC 2.4.1.111 coniferyl-alcohol glucosyltransferase
EC 2.4.1.112 α,1,4-glucan-protein synthase (UDP-forming)
EC 2.4.1.113 α,1,4-glucan-protein synthase (ADP-forming)
EC 2.4.1.114 2-coumarate O-β-glucosyltransferase
EC 2.4.1.115 anthocyanidin 3-O-glucosyltransferase
EC 2.4.1.116 cyanidin 3-O-rutinoside 5-O-glucosyltransferase
EC 2.4.1.117 dolichyl-phosphate β-glucosyltransferase
EC 2.4.1.118 cytokinin 7-β-glucosyltransferase
EC 2.4.1.119 dolichyl—diphosphooligosaccharide-protein glycotransferase
EC 2.4.1.120 sinapate 1-glucosyltransferase
EC 2.4.1.121 indole-3-acetate β-glucosyltransferase
EC 2.4.1.122 glycoprotein-N-acetylgalactosamine 3-β-galactosyltransferase
EC 2.4.1.123 inositol 3-α-galactosyltransferase
EC 2.4.1.124 now included with EC 2.4.1.187
EC 2.4.1.125 sucrose—1,6-α-glucan 3(6)-α-glucosyltransferase
EC 2.4.1.126 hydroxycinnamate 4-β-glucosyltransferase
EC 2.4.1.127 monoterpenol β-glucosyltransferase
EC 2.4.1.128 scopoletin glucosyltransferase
EC 2.4.1.129 peptidoglycan glucosyltransferase
EC 2.4.1.130 dolichyl-phosphate-mannose—glycolipid α-mannosyltransferase
EC 2.4.1.131 glycolipid 2-α-mannosyltransferase
EC 2.4.1.132 glycolipid 3-α-mannosyltransferase
EC 2.4.1.133 xylosylprotein 4-β-galactosyltransferase
EC 2.4.1.134 galactosylxylosylprotein 3-β-galactosyltransferase
EC 2.4.1.135 galactosylgalactosylxylosylprotein 3-β-glucuronosyltransferase
EC 2.4.1.136 gallate 1-β-glucosyltransferase
EC 2.4.1.137 sn-glycerol-3-phosphate 2-α-galactosyltransferase
EC 2.4.1.138 mannnotetraose 2-α-N-acetylgalactosaminyltransferase
EC 2.4.1.139 maltose synthase
EC 2.4.1.140 altamannansucrase
EC 2.4.1.141 N-acetylglucosaminyl-diphosphodiolchol N-acetylglucosaminyltransferase
EC 2.4.1.142 chitobiosydiphosphodiolchol β-mannosyltransferase chitobiosydiphosphodiolchol α-mannosyltransferase
EC 2.4.1.143 α-1,6-mannosyl-glycoprotein 2-β-N-acetylglucosaminyltransferase

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EC 2.4.1.144 β-1,4-mannosyl-glycoprotein 4-β-N-acetylglucosaminyltransferase
EC 2.4.1.145 α-1,3-mannosyl-glycoprotein 4-β-N-acetylglucosaminyltransferase
EC 2.4.1.146 β-1,3-galactosyl-O-glycosyl-glycoprotein β-1,3-N-acetylglucosaminyltransferase
EC 2.4.1.147 acetylgalactosaminyl-O-glycosyl-glycoprotein β-1,3-N-acetylglucosaminyltransferase
EC 2.4.1.148 acetylgalactosaminyl-O-glycosyl-glycoprotein β-1,6-N-acetylglucosaminyltransferase
EC 2.4.1.149 N-acetylactosaminidase β-1,3-N-acetylglucosaminyltransferase
EC 2.4.1.150 N-acetylactosaminidase β-1,6-N-acetylglucosaminyl-transferase
EC 2.4.1.151 included with EC 2.4.1.87
EC 2.4.1.152 galactoside 3-fucosyltransferase
EC 2.4.1.153 dolichyl-phosphate α-N-acetylglucosaminyltransferase
EC 2.4.1.154 now EC 2.4.1.79
EC 2.4.1.155 α-1,6-mannosyl-glycoprotein 6-β-N-acetylglucosaminyltransferase
EC 2.4.1.156 indolylacetyl-β-D-inositol galactosyltransferase
EC 2.4.1.157 1,2-diacylglycerol 3-glucosyltransferase
EC 2.4.1.158 13-hydroxyxycanoate 13-β-glucosyltransferase
EC 2.4.1.159 flavonol-3-O-glycoside L-rhamnosyltransferase
EC 2.4.1.160 pyridoxine 5'-O-β-D-glucosyltransferase
EC 2.4.1.161 oligosaccharide 4-α-D-glucosyltransferase
EC 2.4.1.162 aldehyde β-D-fructosyltransferase
EC 2.4.1.163 β-galactosyl-N-acetylglucosaminylgalactosylglucosyl-ceramide β-1,3-acetylglucosaminyltransferase
EC 2.4.1.164 galactosyl-N-acetylglucosaminylgalactosylglucosyl-ceramide β-1,6-N-acetylglucosaminyltransferase
EC 2.4.1.165 N-acetylneuraminylgalactosylglucosylecramide β-1,4-N-acetylglucosaminyltransferase
EC 2.4.1.166 raffinose—raffinose α-galactosyltransferase
EC 2.4.1.167 sucrose 6'-α-galactosyltransferase
EC 2.4.1.168 xyloglucan 4-glucosyltransferase
EC 2.4.1.169 now EC 2.4.2.39
EC 2.4.1.170 isoflavone 7-O-glucosyltransferase
EC 2.4.1.171 methyl-ONH-azoxymethanol β-D-glucosyltransferase
EC 2.4.1.172 salicyl-alcohol β-D-glucosyltransferase
EC 2.4.1.173 sterol 3β-glucosyltransferase
EC 2.4.1.174 glucuronylgalactosylproteoglycan 4-β-N-acetylglucosaminyltransferase
EC 2.4.1.175 glucuronosyl-N-acetylglactosamine-proteoglycan 4-β-N-acetylglactosaminyltransferase
EC 2.4.1.176 giberrellin β-D-glucosyltransferase
EC 2.4.1.177 cinnamate β-D-glucosyltransferase
EC 2.4.1.178 hydroxymandelonitrile glucosyltransferase
EC 2.4.1.179 lactosylceramide β-1,3-galactosyltransferase
EC 2.4.1.180 lipopolysaccharide N-acetylmannosaminuronosyltransferase
EC 2.4.1.181 hydroxyanthraquinone glucosyltransferase
EC 2.4.1.182 lipid-A-disaccharide synthase
EC 2.4.1.183 α-1,3-glucan synthase
EC 2.4.1.184 galactolipid galactosyltransferase
EC 2.4.1.185 flavanone 7-O-β-glucosyltransferase
EC 2.4.1.186 glycogenin glucosyltransferase
EC 2.4.1.187 N-acetylglucosaminyl2,3-diphosphodecaprenol N-acetyl-β-D-mannosaminyltransferase
EC 2.4.1.188 N-acetylglucosaminyl2,3-diphosphodecaprenol glucosyltransferase
EC 2.4.1.189 luteolin 7-O-glucuronosyltransferase
EC 2.4.1.190 luteolin-7-O-glucuronide 2"-O-glucuronosyltransferase
EC 2.4.1.191 luteolin-7-O-diglucuronide 4"-O-glucuronosyltransferase
EC 2.4.1.192 nontigenin 3β-glycosyltransferase
EC 2.4.1.193 sarsapogenin 3β-glycosyltransferase
EC 2.4.1.194 4-hydroxybenzoate 4-O-β-D-glucosyltransferase
EC 2.4.1.195 N-hydroxythioamide S-β-glucosyltransferase
EC 2.4.1.196 nicotinate glucosyltransferase
EC 2.4.1.197 high-mannose-oligosaccharide β-1,4-N-acetylglucosaminyltransferase
EC 2.4.1.198 phosphatidylinositol N-acetylgalcosaminytransferase
EC 2.4.1.199 β-mannosylphosphodecaprenol—mannooligosaccharide 6-mannosyltransferase
EC 2.4.1.200 α-1,6-mannosyl-glycoprotein 4-β-N-acetylglucosaminyltransferase
EC 2.4.1.202 2,4-dihydroxy-7-methoxy-2H-1,4-benzoxazin-3(4H)-one 2-D-glucosyltransferase
EC 2.4.1.203 trans-zeatin O-β-D-glucosyltransferase
EC 2.4.1.204 galactogen 6β-galactosyltransferase
EC 2.4.1.205 lactosylceramide 1,3-N-acetyl-β-D-galactosaminyltransferase
EC 2.4.1.207 xyloglucan:xyloligosyl transferase
EC 2.4.1.208 diglucosyl diacylglycerol synthase
EC 2.4.1.209 cis-p-coumarate glucosyltransferase
EC 2.4.1.210 limonoid glucosyltransferase
EC 2.4.1.211 1,3-β-galactosyl-N-acetylated hologlucosamine phosphorylase
EC 2.4.1.212 hyaluronan synthase
EC 2.4.1.213 glucosylglycerol-phosphate synthase
EC 2.4.1.214 glycoprotein 3-α-L-fucosyltransferase
EC 2.4.1.215 cis-zeatin O-β-D-glucosyltransferase
EC 2.4.1.216 trehalose 6-phosphate phosphorylase
EC 2.4.1.217 mannosyl-3-phosphoglycerate synthase
EC 2.4.1.218 hydroquinone glucosyltransferase
EC 2.4.1.219 vomilenine glucosyltransferase
EC 2.4.1.220 indoxyl-UDPG glucosyltransferase
EC 2.4.1.221 peptide-O-fucosyltransferase
EC 2.4.1.222 O-fucosylpeptide 3-β-N-acetylglucosaminytransferase
EC 2.4.1.223 glucuronyl-galactosyl-proteoglycan 4-α-N-acetylglucosaminyltransferase
EC 2.4.1.224 glucuronosyl-N-acetylglucosaminyl-proteoglycan 4-α-N-acetylglucosaminyltransferase
EC 2.4.1.226 N-acetylglucosaminyl-proteoglycan 4β-glucuronosyltransferase
EC 2.4.1.227 N-acetylgalactosaminyl-proteoglycan 3β-glucuronosyltransferase
EC 2.4.1.228 undecaprenylphospho-muramoylpentapeptide β-N-acetylglucosaminyltransferase
EC 2.4.1.229 lactosylceramide 4α-galactosyltransferase
EC 2.4.1.229 Skp1-protein)-hydroxyproline N-acetylglucosaminyltransferase
EC 2.4.1.230 kojibiose phosphorylase
EC 2.4.1.231 α,α-trehalose phosphorylase (configuration-retaining)
EC 2.4.1.232 glycolipid 6α-mannosyltransferase
EC 2.4.1.233 deleted now *EC 2.4.1.115
EC 2.4.1.234 kaempferol 3-O-galactosyltransferase
EC 2.4.1.235 now *EC 2.4.1.116
EC 2.4.1.236 flavanone 7-O-glucoside 2"-O-β-L-rhamnosyltransferase
EC 2.4.1.237 flavonol 7-O-β-glucosyltransferase
EC 2.4.1.238 anthocyanin 3'-O-β-glucosyltransferase
EC 2.4.1.239 flavonol-3-O-glucoside glucosyltransferase
EC 2.4.1.240 flavonol-3-O-glycoside glucosyltransferase
EC 2.4.1.241 digalactosyldiacylglycerol synthase
EC 2.4.1.242 NDP-glucose—starch glucosyltransferase
EC 2.4.1.243 6α-fructosyltransferase
EC 2.4.1.244 N-acetylβ-glucosaminyl-glycoprotein 4-β-N-acetylgalactosaminytransferase

EC 2.4 Glycosyltransferases (continued)

EC 2.4.2 Pentosyltransferases
EC 2.4.2.1 purine-nucleoside phosphorylase
EC 2.4.2.2 pyrimidine-nucleoside phosphorylase
EC 2.4.2.3 uridine phosphorylase
EC 2.4.2.4 thymidine phosphorylase
EC 2.4.2.5 nucleoside ribosyltransferase
EC 2.4.2.6 nucleoside deoxyribosyltransferase
EC 2.4.2.7 adenine phosphoribosyltransferase
EC 2.4.2.8 hypoxanthine phosphoribosyltransferase
EC 2.4.2.9 uracil phosphoribosyltransferase
EC 2.4.2.10 orotate phosphoribosyltransferase
EC 2.4.2.11 nicotinate phosphoribosyltransferase
EC 2.4.2.12 nicotinamide phosphoribosyltransferase
EC 2.4.2.13 now EC 2.5.1.6
EC 2.4.2.14 amidophosphoribosyltransferase
EC 2.4.2.15 guanosine phosphorylase
EC 2.4.2.16 urate-ribonucleotide phosphorylase
EC 2.4.2.17 ATP phosphoribosyltransferase
EC 2.4.2.18 anthranilate phosphoribosyltransferase
EC 2.4.2.19 nicotinate-nucleotide diphosphorylase (carboxylating)
EC 2.4.2.20 dioxotetrahdropyrimidine phosphoribosyltransferase
EC 2.4.2.21 nicotinate-nucleotide—dimethylbenzimidazole phosphoribosyltransferase
EC 2.4.2.22 xanthine phosphoribosyltransferase
EC 2.4.2.23 deoxyuridine phosphorylase
EC 2.4.2.24 1,4-β-D-xylan synthase
EC 2.4.2.25 flavone apiosyltransferase
EC 2.4.2.26 protein xylosyltransferase
EC 2.4.2.27 dTDP-dihydropentrose—streptidine-6-phosphate dihydrostreptosyltransferase
EC 2.4.2.28 S-methyl-5′-thiodenosine phosphorylase
EC 2.4.2.29 queuine tRNA-ribosyltransferase
EC 2.4.2.30 NAD′ ADP-ribosyltransferase
EC 2.4.2.31 NAD(P)′—protein-arginine ADP-ribosyltransferase
EC 2.4.2.32 dolichyl-phosphate D-xylosyltransferase
EC 2.4.2.33 dolichyl-xylosyl-phosphate—protein xylosyltransferase
EC 2.4.2.34 indolylacetylinositol arabinosyltransferase
EC 2.4.2.35 flavonol-3-O-glycoside xylosyltransferase
EC 2.4.2.36 NAD′—diphthamide ADP-ribosyltransferase
EC 2.4.2.37 NAD′—dinitrogen-reductase ADP-D-ribosyltransferase
EC 2.4.2.38 glycoprotein 2-β-D-xylosyltransferase
EC 2.4.2.39 xyloglucan 6-xylosyltransferase
EC 2.4.2.40 zeatin O-β-D-xylosyltransferase

EC 2.4.99 Transferring Other Glycosyl Groups

EC 2.4.99.1 β-galactoside α-2,6-sialyltransferase
EC 2.4.99.2 monosialoganglioside sialyltransferase
EC 2.4.99.3 α-N-acetylgalactosaminidase α-2,6-sialyltransferase
EC 2.4.99.4 β-galactoside α-2,3-sialyltransferase
EC 2.4.99.5 galactosylacylglycerol α-2,3-sialyltransferase
EC 2.4.99.6 N-acetylgalactosaminidase α-2,3-sialyltransferase
EC 2.4.99.7 α-N-acetylneuraminyl-2,3-β-galactosyl-1,3-N-acetylegalactosaminide 6-α-sialyltransferase
EC 2.4.99.8 α-N-acetylneuraminidase α-2,8-sialyltransferase
EC 2.4.99.9 lactosylceramide α-2,3-sialyltransferase
EC 2.4.99.10 neolactotetraosylceramide α-2,3-sialyltransferase
EC 2.4.99.11 lactosylceramide α-2,6-N-sialyltransferase
EC 2.5 Transferring Alkyl or Aryl Groups, Other than Methyl Groups

EC 2.5.1.1 dimethylallyltransferase
EC 2.5.1.2 thiamine pyridinyltransferase
EC 2.5.1.3 thiamine-phosphate diphosphorylase
EC 2.5.1.4 adenosylmethionine cyclotransferase
EC 2.5.1.5 galactose-6-sulfurylase
EC 2.5.1.6 methionine adenosyltransferase
EC 2.5.1.7 UDP-N-acetylglucosamine 1-carboxyvinyltransferase
EC 2.5.1.8 tRNA isopentenyltransferase
EC 2.5.1.9 riboflavine synthase
EC 2.5.1.10 geranyltransferase
EC 2.5.1.11 trans-octaprenyltransferase
EC 2.5.1.12 deleted, included in EC 2.5.1.18
EC 2.5.1.13 deleted, included in EC 2.5.1.18
EC 2.5.1.14 deleted, included in EC 2.5.1.18
EC 2.5.1.15 dihydropteroyl synthase
EC 2.5.1.16 spermidine synthase
EC 2.5.1.17 cob(II)ric acid a,c-diamide adenosyltransferase
EC 2.5.1.18 glutathione transferase
EC 2.5.1.19 3-phosphoshikimate 1-carboxyvinyltransferase
EC 2.5.1.20 rubber cis-polyisoprenyltransferase
EC 2.5.1.21 squalene synthase
EC 2.5.1.22 spermine synthase
EC 2.5.1.23 sym-norspermidine synthase
EC 2.5.1.24 discadennine synthase
EC 2.5.1.25 tRNA-uridine aminocarboxypropyltransferase
EC 2.5.1.26 alkylglycerone-phosphate synthase
EC 2.5.1.27 adenylate dimethylallyltransferase
EC 2.5.1.28 dimethylallyltransferase
EC 2.5.1.29 farnesyltransferase
EC 2.5.1.30 trans-hexaprenyltransferase
EC 2.5.1.31 di-trans,poly-cis-decaprenyltransferase
EC 2.5.1.32 phytoene synthase
EC 2.5.1.33 trans-pentaprenyltransferase
EC 2.5.1.34 tryptophan dimethylallyltransferase
EC 2.5.1.35 aspinuline dimethylallyltransferase
EC 2.5.1.36 trihydroxypterocarpan dimethylallyltransferase
EC 2.5.1.37 now EC 4.4.1.20
EC 2.5.1.38 isonocardicin synthase
EC 2.5.1.39 4-hydroxybenzoate nonaprenyltransferase
EC 2.5.1.40 now EC 4.2.3.9
EC 2.5.1.41 phosphoglycerol geranylgeranyltransferase
EC 2.5.1.42 geranylgeranylgeranylgeranyltransferase
EC 2.5.1.43 nicotianamine synthase
EC 2.5.1.44 homospermidine synthase
EC 2.5.1.45 homospermidine synthase (spermidine-specific)
EC 2.5.1.46 deoxyhypusine synthase
EC 2.5.1.47 cysteine synthase
EC 2.5.1.48 cystathionine γ-synthase
EC 2.5.1.49 O-acetylhomoserine aminocarboxypropyltransferase
EC 2.5.1.50 zeatin 9-aminocarboxyethyltransferase
EC 2.5.1.51 β-pyrrozolylaniline synthase
EC 2.5.1.52 L-mimosine synthase
EC 2.5.1.53 uracyllalanine synthase
EC 2.5.1.54 3-deoxy-7-phosphoheptulonate synthase
EC 2.5.1.55 3-deoxy-8-phosphoheptulonate synthase
EC 2.5.1.56 N-acetylneuraminic synthase
EC 2.5.1.57 N-acetylneuraminic-9-phosphate synthase
EC 2.5.1.58 protein farnesyltransferase
EC 2.5.1.59 protein geranylgeranyltransferase type I
EC 2.5.1.60 protein geranylgeranyltransferase type II
EC 2.5.1.61 hydroxymethylbilane synthase
EC 2.5.1.62 chlorophyll synthase
EC 2.5.1.63 adenosyl-fluoride synthase
EC 2.5.1.64 2-succinyl-6-hydroxyhexa-2,4-diene-1-carboxylate synthase
EC 2.5.1.65 O-phosphoserine sulfhydrlyase
EC 2.5.1.66 N2-(2-carboxyethyl)arginine synthase

EC 2.6 Transferring Nitrogenous Groups

EC 2.6.1 Transaminases

EC 2.6.1.1 aspartate transaminase
EC 2.6.1.2 alanine transaminase
EC 2.6.1.3 cysteine transaminase
EC 2.6.1.4 glycine transaminase
EC 2.6.1.5 tyrosine transaminase
EC 2.6.1.6 leucine transaminase
EC 2.6.1.7 kynurenine—oxoglutarate transaminase
EC 2.6.1.8 2,5-diaminovlerate transaminase
EC 2.6.1.9 histidinol-phosphate transaminase
EC 2.6.1.10 deleted, included in EC 2.6.1.21
EC 2.6.1.11 acetylornithine transaminase
EC 2.6.1.12 alanine—oxo-acid transaminase
EC 2.6.1.13 ornithine aminotransferase
EC 2.6.1.14 asparagine—oxo-acid transaminase
EC 2.6.1.15 glutamine—pyruvate transaminase
EC 2.6.1.16 glutamine—fructose-6-phosphate transaminase (isomerizing)
EC 2.6.1.17 succinylidiaminopimelate transaminase
EC 2.6.1.18 β-alanine—pyruvate transaminase
EC 2.6.1.19 4-aminobutyrate transaminase
EC 2.6.1.20 deleted
EC 2.6.1.21 D-amino acid transaminase
EC 2.6.1.22 (S)-3-amino-2-methylpropionate transaminase
EC 2.6.1.23 4-hydroxyglutamate transaminase
EC 2.6.1.24 diiodotyrosine transaminase
EC 2.6.1.25 deleted, included in EC 2.6.1.24
EC 2.6.1.26 thyroid-hormone transaminase
EC 2.6.1.27 tryptophan transaminase
EC 2.6.1.28 tryptophan—phenylpyruvate transaminase
EC 2.6.1.29 diamine transaminase
EC 2.6.1.30 pyridoxamine—pyruvate transaminase
EC 2.6.1.31 pyridoxamine—oxaloacetate transaminase
EC 2.6.1.32 valine—3-methyl-2-oxovalerate transaminase
EC 2.6.1.33 dTDP-4-amino-4,6-dideoxy-D-glucose transaminase
EC 2.6.1.34 UDP-2-acetamido-4-amino-2,4,6-trideoxyglucose transaminase
EC 2.6.1.35 glycine—oxaloacetate transaminase
EC 2.6.1.36 L-lysine 6-transaminase
EC 2.6.1.37 (2-aminoethyl)phosphonate—pyruvate transaminase
EC 2.6.1.38 histidine transaminase
EC 2.6.1.39 2-amino adipate transaminase
EC 2.6.1.40 (R)-3-amino-2-methylpropionate—pyruvate transaminase
EC 2.6.1.41 D-methionine—pyruvate transaminase
EC 2.6.1.42 branched-chain-amino-acid transaminase
EC 2.6.1.43 aminolevulinate transaminase
EC 2.6.1.44 alanine—glyoxylate transaminase
EC 2.6.1.45 serine—glyoxylate transaminase
EC 2.6.1.46 diaminobutyrate—pyruvate transaminase
EC 2.6.1.47 alanine—oxomalonate transaminase
EC 2.6.1.48 5-aminovalerate transaminase
EC 2.6.1.49 dihydroxyphenylalanine transaminase
EC 2.6.1.50 glutamine—scyllo-inositol transaminase
EC 2.6.1.51 serine—pyruvate transaminase
EC 2.6.1.52 phosphoserine transaminase
EC 2.6.1.53 now EC 1.4.1.13
EC 2.6.1.54 pyridoxamine-phosphate transaminase
EC 2.6.1.55 taurine—2-oxoglutarate transaminase
EC 2.6.1.56 1D-1-guanidino-3-amino-1,3-dideoxy-scyllo-inositol transaminase
EC 2.6.1.57 aromatic-amino-acid transaminase
EC 2.6.1.58 phenylalanine(histidine) transaminase
EC 2.6.1.59 dTDP-4-amino-4,6-dideoxygalactose transaminase
EC 2.6.1.60 aromatic-amino-acid—glyoxylate transaminase
EC 2.6.1.61 identical to EC 2.6.1.40
EC 2.6.1.62 adenosylmethionine—8-amino-7-oxononanoate transaminase
EC 2.6.1.63 kynurenine—glyoxylate transaminase
EC 2.6.1.64 glutamine—phenylpyruvate transaminase
EC 2.6.1.65 N'-acetyl-β-lysine transaminase
EC 2.6.1.66 valine—pyruvate transaminase
EC 2.6.1.67 2-amino hexanoate transaminase
EC 2.6.1.68 ornithine(lysine) transaminase
EC 2.6.1.69 now EC 2.6.1.11
EC 2.6.1.70 aspartate—phenylpyruvate transaminase
EC 2.6.1.71 lysine—pyruvate 6-transaminase
EC 2.6.1.72 D-4-hydroxyphenylglycine transaminase
EC 2.6.1.73 methionine—glyoxylate transaminase
EC 2.6.1.74 cephalosporin-C transaminase
EC 2.6.1.75 cysteine-conjugate transaminase
EC 2.6.1.76 diaminobutyrate—2-oxoglutarate transaminase
EC 2.6.1.77 taurine—pyruvate aminotransferase
EC 2.6.1.78 asparagine—phenylalanine aminotransferase
EC 2.6.1.79 glutamate—prephenate aminotransferase
EC 2.6.1.80 nicotianamide aminotransferase
EC 2.6.1.81 succinylornithine transaminase
EC 2.6.1.82 putrescine aminotransferase
EC 2.6.1.83 LL-diaminopimelate aminotransferase

EC 2.6.2 Amidinotransferases

EC 2.6.2.1 now EC 2.1.4.1

EC 2.6.3 Oximino transferases
EC 2.6.3.1 oximinotransferase

2.6.99 Transferring Other Nitrogenous Groups

EC 2.6.99.1 dATP(dGTP)—DNA purinetransferase
EC 2.6.99.2 pyridoxine 5'-phosphate synthase

EC 2.7 Transferring Phosphorus-Containing Groups

EC 2.7.1 Phosphotransferases with an Alcohol Group as Acceptor

EC 2.7.1.1 hexokinase
EC 2.7.1.2 glucokinase
EC 2.7.1.3 ketohexokinase
EC 2.7.1.4 fructokinase
EC 2.7.1.5 rhamnulokinase
EC 2.7.1.6 galactokinase
EC 2.7.1.7 mannokinase
EC 2.7.1.8 glucosamine kinase
EC 2.7.1.9 deleted
EC 2.7.1.10 phosphoglucomutase
EC 2.7.1.11 6-phosphofructokinase
EC 2.7.1.12 gluconokinase
EC 2.7.1.13 dehydrogluconokinase
EC 2.7.1.14 sedoheptulokinase
EC 2.7.1.15 ribokinase
EC 2.7.1.16 ribulokinase
EC 2.7.1.17 xylulokinase
EC 2.7.1.18 phosphoribokinase
EC 2.7.1.19 phosphoribulokinase
EC 2.7.1.20 adenosine kinase
EC 2.7.1.21 thymidine kinase
EC 2.7.1.22 ribosyl-adenosine kinase
EC 2.7.1.23 NAD+ kinase
EC 2.7.1.24 dephospho-CoA kinase
EC 2.7.1.25 adenyl-sulfate kinase
EC 2.7.1.26 riboflavin kinase
EC 2.7.1.27 erythritol kinase
EC 2.7.1.28 triokinase
EC 2.7.1.29 glyceraldehyde kinase
EC 2.7.1.30 glycerol kinase
EC 2.7.1.31 glycerate kinase
EC 2.7.1.32 choline kinase
EC 2.7.1.33 pantothenate kinase
EC 2.7.1.34 pantetheine kinase
EC 2.7.1.35 pyridoxal kinase
EC 2.7.1.36 nevalonate kinase
EC 2.7.1.37 now divided into EC 2.7.11.1, EC 2.7.11.8, EC 2.7.11.9, EC 2.7.11.10, EC 2.7.11.11, EC 2.7.11.12, EC 2.7.11.13, EC 2.7.11.21, EC 2.7.11.22, EC 2.7.11.24, EC 2.7.11.25, EC 2.7.11.30 and EC 2.7.12.1
EC 2.7.1.38 now EC 2.7.11.19
EC 2.7.1.39 homoserine kinase
EC 2.7.1.40 pyruvate kinase
EC 2.7.1.41 glucose-1-phosphate phosphomutase
EC 2.7.1.42 riboflavin phosphotransferase
EC 2.7.1.43 glucuronokinase
EC 2.7.1.44 galacturonokinase
EC 2.7.1.45 2-dehydro-3-deoxygluconokinase
EC 2.7.1.46 L-arabinokinase
EC 2.7.1.47 D-ribulokinase
EC 2.7.1.48 uridine kinase
EC 2.7.1.49 hydroxymethylpyrimidine kinase
EC 2.7.1.50 hydroxyethylthiazole kinase
EC 2.7.1.51 L-fucokinase
EC 2.7.1.52 fucokinase
EC 2.7.1.53 L-xylulokinase
EC 2.7.1.54 D-arabinokinase
EC 2.7.1.55 allose kinase
EC 2.7.1.56 1-phosphofructokinase
EC 2.7.1.57 deleted
EC 2.7.1.58 2-dehydro-3-deoxygalactonokinase
EC 2.7.1.59 N-acetylglucosamine kinase
EC 2.7.1.60 N-acetylmannosamine kinase
EC 2.7.1.61 acyl-phosphate—hexose phosphotransferase
EC 2.7.1.62 phosphorimidate—hexose phosphotransferase
EC 2.7.1.63 polyphosphate—glucose phosphotransferase
EC 2.7.1.64 inositol 3-kinase
EC 2.7.1.65 scyllo-inosamine 4-kinase
EC 2.7.1.66 undecaprenol kinase
EC 2.7.1.67 1-phosphatidylinositol 4-kinase
EC 2.7.1.68 1-phosphatidylinositol-4-phosphate 5-kinase
EC 2.7.1.69 protein-A'-phosphohistidine—sugar phosphotransferase
EC 2.7.1.70 identical to EC 2.7.1.37
EC 2.7.1.70 protamine kinase
EC 2.7.1.71 shikimate kinase
EC 2.7.1.72 streptomycin 6-kinase
EC 2.7.1.73 inosine kinase
EC 2.7.1.74 deoxyeytidine kinase
EC 2.7.1.75 new EC 2.7.1.21
EC 2.7.1.76 deoxyadenosine kinase
EC 2.7.1.77 nucleoside phosphotransferase
EC 2.7.1.78 polynucleotide 5'-hydroxyl-kinase
EC 2.7.1.79 diphosphate—glycerol phosphotransferase
EC 2.7.1.80 diphosphate—serine phosphotransferase
EC 2.7.1.81 hydroxyllysine kinase
EC 2.7.1.82 ethanolamine kinase
EC 2.7.1.83 pseudouridine kinase
EC 2.7.1.84 alklyglycerone kinase
EC 2.7.1.85 β-glucoside kinase
EC 2.7.1.86 NADH kinase
EC 2.7.1.87 streptomycin 3''-kinase
EC 2.7.1.88 dihydrostreptomycin-6-phosphate 3''-kinase
EC 2.7.1.89 thiamine kinase
EC 2.7.1.90 diphosphate—fructose-6-phosphate 1-phosphotransferase
EC 2.7.1.91 sphingamine kinase
EC 2.7.1.92 5-dehydro-2-deoxygluconokinase
EC 2.7.1.93 alklyglycerol kinase
EC 2.7.1.94 acylglycerol kinase
EC 2.7.1.95 kanamycin kinase
EC 2.7.1.96 deleted, included in EC 2.7.1.86
EC 2.7.1.97 deleted, identical to EC 2.7.1.125
EC 2.7.1.98 deleted
EC 2.7.1.99 now EC 2.7.11.2
EC 2.7.1.100 S-methyl-5-thioribose kinase
EC 2.7.1.101 tagatose kinase
EC 2.7.1.102 hamamelose kinase
EC 2.7.1.103 viomycin kinase
EC 2.7.1.104 now EC 2.7.99.1
EC 2.7.1.105 6-phosphofructo-2-kinase
EC 2.7.1.106 glucose-1,6-bisphosphate synthase
EC 2.7.1.107 diacylglycerol kinase
EC 2.7.1.108 dolichol kinase
EC 2.7.1.109 now EC 2.7.11.31
EC 2.7.1.110 now EC 2.7.11.3
EC 2.7.1.111 now EC 2.7.1.128
EC 2.7.1.112 now EC 2.7.10.1 and EC 2.7.10.2
EC 2.7.1.113 deoxyguanosine kinase
EC 2.7.1.114 AMP—thymidine kinase
EC 2.7.1.115 now EC 2.7.11.4
EC 2.7.1.116 now EC 2.7.11.5
EC 2.7.1.117 now EC 2.7.11.18
EC 2.7.1.118 ADP—thymidine kinase
EC 2.7.1.119 hygromycin-B kinase
EC 2.7.1.120 now part of EC 2.7.11.17
EC 2.7.1.121 phosphoenolpyruvate—glycerone phosphotransferase
EC 2.7.1.122 xylitol kinase
EC 2.7.1.123 now part of EC 2.7.11.17
EC 2.7.1.124 now EC 2.7.11.6
EC 2.7.1.125 now EC 2.7.11.14
EC 2.7.1.126 now EC 2.7.11.15
EC 2.7.1.127 inositol-trisphosphate 3-kinase
EC 2.7.1.128 now EC 2.7.11.27
EC 2.7.1.129 now EC 2.7.11.7
EC 2.7.1.130 tetraacyldisaccharide 4'-kinase
EC 2.7.1.131 now EC 2.7.11.29
EC 2.7.1.132 now EC 2.7.11.28
EC 2.7.1.133 now with EC 2.7.1.134
EC 2.7.1.134 inositol-tetrakisphosphate 1-kinase
EC 2.7.1.135 now EC 2.7.11.26
EC 2.7.1.136 macrolide 2'-kinase
EC 2.7.1.137 phospatidylinositol 3-kinase
EC 2.7.1.138 ceramide kinase
EC 2.7.1.139 now with EC 2.7.1.134
EC 2.7.1.140 inositol-tetrakisphosphate 5-kinase
EC 2.7.1.141 now EC 2.7.11.23
EC 2.7.1.142 glycerol—3-phosphate-glucose phosphotransferase
EC 2.7.1.143 diphosphate-purine nucleoside kinase
EC 2.7.1.144 tagatose-6-phosphate kinase
EC 2.7.1.145 deoxynucleoside kinase
EC 2.7.1.146 ADP-dependent phosphofructokinase
EC 2.7.1.147 ADP-dependent glucokinase
EC 2.7.1.148 4-(cytidine 5'-diphospho)-2-C-methyl-D-erythrithol kinase
EC 2.7.1.149 1-phosphatidylinositol-5-phosphate 4-kinase
EC 2.7.1.150 1-phosphatidylinositol-3-phosphate 5-kinase
EC 2.7.1.151 inositol-polyphosphate multikinase
EC 2.7.1.152 now EC 2.7.4.21
EC 2.7.1.153 phosphatidylinositol-4,5-bisphosphate 3-kinase
EC 2.7.1.154 phosphatidylinositol-4-phosphate 3-kinase
EC 2.7.1.155 diphasphoinositol-pentakisphosphate kinase
EC 2.7.1.156 adenosylcobinamide kinase
EC 2.7.1.157 N-acetylgalactosamine kinase
EC 2.7.1.158 inositol-pentakisphosphate 2-kinase
EC 2.7.1.159 inositol-1,3,4-trisphosphate 5/6-kinase
EC 2.7.1.160 2'-phosphotransferase

**EC 2.7.2 Phosphotransferases with a carboxy group as acceptor**

EC 2.7.2.1 acetate kinase
EC 2.7.2.2 carbamate kinase
EC 2.7.2.3 phosphoglycerate kinase
EC 2.7.2.4 aspartate kinase
EC 2.7.2.5 now EC 6.3.4.16
EC 2.7.2.6 formate kinase
EC 2.7.2.7 butyrate kinase
EC 2.7.2.8 acetylglutamate kinase
EC 2.7.2.9 now EC 6.3.5.5
EC 2.7.2.10 phosphoglycerate kinase (GTP)
EC 2.7.2.11 glutamate 5-kinase
EC 2.7.2.12 acetate kinase (diphosphate)
EC 2.7.2.13 glutamate 1-kinase
EC 2.7.2.14 branched-chain-fatty-acid kinase
EC 2.7.2.15 propionate kinase

**EC 2.7.3 Phosphotransferases with a nitrogenous group as acceptor**

EC 2.7.3.1 guanidinoacetate kinase
EC 2.7.3.2 creatine kinase
EC 2.7.3.3 arginine kinase
EC 2.7.3.4 taurocyamine kinase
EC 2.7.3.5 lombricine kinase
EC 2.7.3.6 hypotaurocyamine kinase
EC 2.7.3.7 opheline kinase
EC 2.7.3.8 ammonia kinase
EC 2.7.3.9 phosphoenolpyruvate—protein phosphotransferase
EC 2.7.3.10 agmatine kinase
EC 2.7.3.11 now EC 2.7.13.1
EC 2.7.3.12 now EC 2.7.13.2

**EC 2.7.4 Phosphotransferases with a phosphate group as acceptor**

EC 2.7.4.1 polyphosphate kinase
EC 2.7.4.2 phosphomevalonate kinase
EC 2.7.4.3 adenylate kinase
EC 2.7.4.4 nucleoside-phosphate kinase
EC 2.7.4.5 deleted, included in EC 2.7.4.14
EC 2.7.4.6 nucleoside-diphosphate kinase
EC 2.7.4.7 phosphomethylpyrimidine kinase
EC 2.7.4.8 guanylinate kinase
EC 2.7.4.9 dTMP kinase
EC 2.7.4.10 nucleoside-triphosphate—adenylate kinase
EC 2.7.4.11 (deoxy)adenylate kinase
EC 2.7.4.12 T<sub>3</sub>-induced deoxynucleotide kinase
EC 2.7.4.13 (deoxy)nucleoside-phosphate kinase
EC 2.7.4.14 cytidylyl kinase
EC 2.7.4.15 thiamine-diphosphate kinase
EC 2.7.4.16 thiamine-phosphate kinase
EC 2.7.4.17 3-phosphoglyceroyl-phosphate—polyphosphate phosphotransferase
EC 2.7.4.18 farnesyl-diphosphate kinase
EC 2.7.4.19 5-methyldeoxycytidine-5′-phosphate kinase
EC 2.7.4.20 dolichyl-diphosphate—polyphosphate phosphotransferase
EC 2.7.4.21 inositol-hexakisphosphate kinase
EC 2.7.4.22 UMP kinase
EC 2.7.4.23 ribose 1,5-bisphosphate phosphokinase

EC 2.7.5 Phosphotransferases with regeneration of donors, apparently catalysing intramolecular transfers

EC 2.7.5.1 now EC 5.4.2.2
EC 2.7.5.2 now EC 5.4.2.3
EC 2.7.5.3 now EC 5.4.2.1
EC 2.7.5.4 now EC 5.4.2.4
EC 2.7.5.5 now EC 5.4.2.5
EC 2.7.5.6 now EC 5.4.2.7
EC 2.7.5.7 now EC 5.4.2.8

EC 2.7.6 Diphosphotransferases

EC 2.7.6.1 ribose-phosphate diphosphokinase
EC 2.7.6.2 thiamine diphosphokinase
EC 2.7.6.3 2-amino-4-hydroxy-6-hydroxymethylidihydropteridine diphosphokinase
EC 2.7.6.4 nucleotide diphosphokinase
EC 2.7.6.5 GTP diphosphokinase

EC 2.7.7 Nucleotidyldtransferases

EC 2.7.7.1 nicotinamide-nucleotide adenyllyltransferase
EC 2.7.7.2 FMN adenyllyltransferase
EC 2.7.7.3 pantetheine-phosphate adenyllyltransferase
EC 2.7.7.4 sulfate adenyllyltransferase
EC 2.7.7.5 sulfate adenyllyltransferase (ADP)
EC 2.7.7.6 DNA-directed RNA polymerase
EC 2.7.7.7 DNA-directed DNA polymerase
EC 2.7.7.8 polyribonucleotide nucleotidyldtransferase
EC 2.7.7.9 UTP—glucose-1-phosphate uridylyltransferase
EC 2.7.7.10 UTP—hexose-1-phosphate uridylyltransferase
EC 2.7.7.11 UTP—xylose-1-phosphate uridylyltransferase
EC 2.7.7.12 UDP—glucose—hexose-1-phosphate uridylyltransferase
EC 2.7.7.13 mannose-1-phosphate guanylyltransferase
EC 2.7.7.14 ethanolamine-phosphate cytidylyltransferase
EC 2.7.7.15 choline-phosphate cytidylyltransferase
EC 2.7.7.16 now EC 3.1.27.5
EC 2.7.7.17 now EC 3.1.27.1
EC 2.7.7.18 nicotinate-nucleotide adenyllytransferase
EC 2.7.7.19 polymonucleotide adenyllytransferase
EC 2.7.7.20 deleted
EC 2.7.7.21 tRNA cytidylytransferase
EC 2.7.7.22 mannose-1-phosphate guanylyltransferase (GDP)
EC 2.7.7.23 UDP-N-acetylgalactosamine diphosphorylase
EC 2.7.7.24 glucose-1-phosphate thymidylytransferase
EC 2.7.7.25 tRNA adenyllytransferase
EC 2.7.7.26 now EC 3.1.27.3
EC 2.7.7.27 glucose-1-phosphate adenyllytransferase
EC 2.7.7.28 nucleoside-triphosphate-hexose-1-phosphate nucleotidyltransferase
EC 2.7.7.29 identical to EC 2.7.7.28
EC 2.7.7.30 fucose-1-phosphate guanylyltransferase
EC 2.7.7.31 DNA nucleotidylexotransferase
EC 2.7.7.32 galactose-1-phosphate thymidylytransferase
EC 2.7.7.33 glucose-1-phosphate cytidylytransferase
EC 2.7.7.34 glucose-1-phosphate guanylyltransferase
EC 2.7.7.35 ribose-5-phosphate adenyllytransferase
EC 2.7.7.36 aldose-1-phosphate adenyllytransferase
EC 2.7.7.37 aldose-1-phosphate nucleotidyltransferase
EC 2.7.7.38 3-deoxy-manno-octulosonate cytidylyltransferase
EC 2.7.7.39 glycerol-3-phosphate cytidylyltransferase
EC 2.7.7.40 D-ribitol-5-phosphate cytidylyltransferase
EC 2.7.7.41 phosphatidate cytidylyltransferase
EC 2.7.7.42 [glutamate—ammonia-ligase] adenyllytransferase
EC 2.7.7.43 N-acetylneuraminic cytidylyltransferase
EC 2.7.7.44 glucuronate-1-phosphate uridylyltransferase
EC 2.7.7.45 guanosine-triphosphate guanylyltransferase
EC 2.7.7.46 gentamicin 2"-nucleotidyltransferase
EC 2.7.7.47 streptomycin 3"-adenyllytransferase
EC 2.7.7.48 RNA-directed RNA polymerase
EC 2.7.7.49 RNA-directed DNA polymerase
EC 2.7.7.50 mRNA guanylyltransferase
EC 2.7.7.51 adenylyl-sulfate—ammonia adenyllytransferase
EC 2.7.7.52 RNA uridylyltransferase
EC 2.7.7.53 ATP adenyllytransferase
EC 2.7.7.54 phenylalanine adenyllytransferase
EC 2.7.7.55 anthranilate adenyllytransferase
EC 2.7.7.56 tRNA nucleotidyltransferase
EC 2.7.7.57 N-methylphosphoethanolamine cytidylyltransferase
EC 2.7.7.58 (2,3-dihydroxybenzoyl)adenylate synthase
EC 2.7.7.59 [protein-PII] uridylyltransferase
EC 2.7.7.60 2-C-methyl-D-erythritol 4-phosphate cytidylyltransferase
EC 2.7.7.61 holo-ACP synthase
EC 2.7.7.62 adenosylcobinamide-phosphate guanylyltransferase
EC 2.7.7.63 lipoate—protein ligase

EC 2.7.8 Transferases for other substituted phosphate groups

EC 2.7.8.1 ethanolaminephosphotransferase
EC 2.7.8.2 diacylglycerol cholinephosphotransferase
EC 2.7.8.3 ceramide cholinephosphotransferase
EC 2.7.8.4 serine-phosphoethanolamine synthase
EC 2.7.8.5 CDP-diacylglycerol-glycerol-3-phosphate 3-phosphatidyltransferase
EC 2.7.8.6 undecaprenyl-phosphate galactose phosphotransferase
EC 2.7.8.7 holo-[acyl-carrier-protein] synthase
EC 2.7.8.8 CDP-diacylglycerol—serine O-phosphatidyltransferase
EC 2.7.8.9 phosphomannan mannosephosttransferase
EC 2.7.8.10 sphingosine cholinephosphotransferase
EC 2.7.8.11 CDP-diacylglycerol—inositol 3-phosphatidyltransferase
EC 2.7.8.12 CDP-glycerol glycerophosphotransferase
EC 2.7.8.13 phospho-N-acetylmuramoyl-pentapeptide-transferase
EC 2.7.8.14 CDP-ribitol ribitolphosphotransferase
EC 2.7.8.15 UDP-N-acetylgalactosamine—dolichyl-phosphate N-acetylgalcosaminephosphotransferase
EC 2.7.8.16 deleted, included in EC 2.7.8.2
EC 2.7.8.17 UDP-N-acetylgalactosamine—lysosomal enzyme N-acetylgalactosaminephotransferase
EC 2.7.8.18 UDP-galactose—UDP-N-acetylgalactosamine galactose phototransferase
EC 2.7.8.19 UDP-glucose—glycoprotein glucos phosphotransferase
EC 2.7.8.20 phosphatidylglycerol—membrane-oligosaccharide glycerophosphotransferase
EC 2.7.8.21 membrane-oligosaccharide glycerophosphotransferase
EC 2.7.8.22 1-alkenyl-2-acetylcerol choline phototransferase
EC 2.7.8.23 carboxyvinyl-carboxyphosphonate phosphorylmutase
EC 2.7.8.24 phosphorylcholine synthase
EC 2.7.8.25 triphosphoribosyl-dephospho-CoA synthase
EC 2.7.8.26 adenosylcobinamide-GDP ribazoletransferase

**EC 2.7.9 Phosphotransferases with paired acceptors**

EC 2.7.9.1 pyruvate, phosphate dikinase
EC 2.7.9.2 pyruvate, water dikinase
EC 2.7.9.3 selenide, water dikinase
EC 2.7.9.4 α-glucan, water dikinase
EC 2.7.9.5 phosphoglucan, water dikinase

**EC 2.7.10 Protein-tyrosine kinases**

EC 2.7.10.1 receptor protein-tyrosine kinase
EC 2.7.10.2 non-specific protein-tyrosine kinase

**EC 2.7.11 Protein-serine/threonine kinases**

EC 2.7.11.1 non-specific serine/threonine protein kinase
EC 2.7.11.2 [pyruvate dehydrogenase (acetyl-transferring)] kinase
EC 2.7.11.3 dephospho-[reductase kinase] kinase
EC 2.7.11.4 [3-methyl-2-oxobutanoate dehydrogenase (acetyl-transferring)] kinase
EC 2.7.11.5 [isocitrate dehydrogenase (NADP⁺)] kinase
EC 2.7.11.6 [tyrosine 3-monoxygenase] kinase
EC 2.7.11.7 myosin-heavy-chain kinase
EC 2.7.11.8 Fas-activated serine/threonine kinase
EC 2.7.11.9 Goodpasture-antigen-binding protein kinase
EC 2.7.11.10 IkB kinase
EC 2.7.11.11 cAMP-dependent protein kinase
EC 2.7.11.12 cGMP-dependent protein kinase
EC 2.7.11.13 protein kinase C
EC 2.7.11.14 rhodopsin kinase
EC 2.7.11.15 β-adrenergic-receptor kinase
EC 2.7.11.16 G-protein-coupled receptor kinase
EC 2.7.11.17 Ca²⁺/calmodulin-dependent protein kinase
EC 2.7.11.18 myosin-light-chain kinase
EC 2.7.11.19 phosphorylase kinase
EC 2.7.11.20 elongation factor 2 kinase
EC 2.7.11.21 polo kinase
EC 2.7.11.22 cyclin-dependent kinase
EC 2.7.11.23 [RNA-polymerase]-subunit kinase
EC 2.7.11.24 mitogen-activated protein kinase
EC 2.7.11.25 mitogen-activated protein kinase kinase kinase
EC 2.7.11.26 tau-protein kinase
EC 2.7.11.27 [acetyl-CoA carboxylase] kinase
EC 2.7.11.28 tropomyosin kinase
EC 2.7.11.29 low-density-lipoprotein receptor kinase
EC 2.7.11.30 receptor protein serine/threonine kinase
EC 2.7.11.31 [hydroxymethylglutaryl-CoA reductase (NADPH)] kinase

**EC 2.7.12 Dual-specificity kinases** (those acting on Ser/Thr and Tyr residues)

EC 2.7.12.1 dual-specificity kinase
EC 2.7.12.2 mitogen-activated protein kinase kinase

**EC 2.7.13 Protein-histidine kinases**

EC 2.7.13.1 protein-histidine pros-kinase
EC 2.7.13.2 protein-histidine tele-kinase
EC 2.7.13.3 histidine kinase

**EC 2.7.99 Other protein kinases**

EC 2.7.99.1 triphosphate—protein phosphotransferase

**EC 2.8 Transferring Sulfur-Containing Groups**

**EC 2.8.1 Sulfurtransferases**

EC 2.8.1.1 thiosulfate sulfurtransferase
EC 2.8.1.2 3-mercaptopyruvate sulfurtransferase
EC 2.8.1.3 thiosulfate—thiol sulfurtransferase
EC 2.8.1.4 tRNA sulfurtransferase
EC 2.8.1.5 thiosulfate—dithiol sulfurtransferase
EC 2.8.1.6 biotin synthase
EC 2.8.1.7 cysteine desulfurase
EC 2.8.1.8 lipooyl synthase

**EC 2.8.2 Sulfotransferases**

EC 2.8.2.1 aryl sulfotransferase
EC 2.8.2.2 alcohol sulfotransferase
EC 2.8.2.3 amine sulfotransferase
EC 2.8.2.4 estrone sulfotransferase
EC 2.8.2.5 chondroitin 4-sulfotransferase
EC 2.8.2.6 choline sulfotransferase
EC 2.8.2.7 UDP-N-acetylgalactosamine-4-sulfate sulfotransferase
EC 2.8.2.8 desulfoparvin sulfotransferase
EC 2.8.2.9 tyrosine-ester sulfotransferase
EC 2.8.2.10 Renilla-luciferin sulfotransferase
EC 2.8.2.11 galactosylceramide sulfotransferase
EC 2.8.2.12 identical to EC 2.8.2.8
EC 2.8.2.13 psychosine sulfotransferase
EC 2.8.2.14 bile-salt sulfotransferase
EC 2.8.2.15 steroid sulfotransferase
EC 2.8.2.16 thiol sulfotransferase
EC 2.8.2.17 chondroitin 6-sulfotransferase
EC 2.8.2.18 cortisol sulfotransferase
EC 2.8.2.19 triglucosylalkylacylglycerol sulfotransferase
EC 2.8.2.20 protein-tyrosine sulfotransferase
EC 2.8.2.21 keratan sulfotransferase
EC 2.8.2.22 aryl-sulfate sulfotransferase
EC 2.8.2.23 [heparan sulfate]-glucosamine 3-sulfotransferase 1
EC 2.8.2.24 desulfoglucosinolate sulfotransferase
EC 2.8.2.25 flavonol 3-sulfotransferase
EC 2.8.2.26 quercetin-3-sulfate 3'-sulfotransferase
EC 2.8.2.27 quercetin-3-sulfate 4'-sulfotransferase
EC 2.8.2.28 quercetin-3,3'-bissulfate 7-sulfotransferase
EC 2.8.2.29 [heparan sulfate]-glucosamine 3-sulfotransferase 2
EC 2.8.2.30 [heparan sulfate]-glucosamine 3-sulfotransferase 3
EC 2.8.2.31 petromyzonol sulfotransferase
EC 2.8.2.32 scymnol sulfotransferase
EC 2.8.2.33 N-acetylgalactosamine 4-sulfate 6-O-sulfotransferase
EC 2.8.2.34 glycochenodeoxycholate sulfotransferase

EC 2.8.3 CoA-transferases

EC 2.8.3.1 propionate CoA-transferase
EC 2.8.3.2 oxalate CoA-transferase
EC 2.8.3.3 malonate CoA-transferase
EC 2.8.3.4 deleted
EC 2.8.3.5 3-oxoacid CoA-transferase
EC 2.8.3.6 3-oxoadipate CoA-transferase
EC 2.8.3.7 succinate—citramalate CoA-transferase
EC 2.8.3.8 acetate CoA-transferase
EC 2.8.3.9 butyrate—acetoacetate CoA-transferase
EC 2.8.3.10 citrate CoA-transferase
EC 2.8.3.11 citramalate CoA-transferase
EC 2.8.3.12 glutaconate CoA-transferase
EC 2.8.3.13 succinate—hydroxymethylglutarate CoA-transferase
EC 2.8.3.14 5-hydroxypentanoate CoA-transferase
EC 2.8.3.15 succinyl-CoA;(R)-benzylsuccinate CoA-transferase
EC 2.8.3.16 formyl-CoA transferase
EC 2.8.3.17 cinnamoyl-CoA:phenyllactate CoA-transferase

EC 2.8.4 Transferring alkylthio groups

EC 2.8.4.1 coenzyme-B sulfoethylthiotransferase

EC 2.9 Transferring Selenium-Containing Groups

EC 2.9.1 Selenotransferases

EC 2.9.1.1 L-seryl-tRNA\textsuperscript{sec} selenium transferase
EC 3. Hydrolases

EC 3.1 Acting on Ester Bonds

**EC 3.1.1 Carboxylic Ester Hydrolases**

EC 3.1.1.1 carboxylesterase
EC 3.1.1.2 arylesterase
EC 3.1.1.3 triacylglycerol lipase
EC 3.1.1.4 phospholipase A₂
EC 3.1.1.5 lysophospholipase
EC 3.1.1.6 acetylesterase
EC 3.1.1.7 acetylcholinesterase
EC 3.1.1.8 cholinesterase
EC 3.1.1.9 deleted
EC 3.1.1.10 tropinesterase
EC 3.1.1.11 pectinesterase
EC 3.1.1.12 deleted
EC 3.1.1.13 sterol esterase
EC 3.1.1.14 chlorophyllase
EC 3.1.1.15 L-arabinonolactonase
EC 3.1.1.16 deleted, mixture of EC 5.3.3.4 and EC 3.1.1.24
EC 3.1.1.17 gluconolactonase
EC 3.1.1.18 deleted, included in EC 3.1.1.17
EC 3.1.1.19 uronolactonase
EC 3.1.1.20 tannase
EC 3.1.1.21 retinyl-palmitate esterase
EC 3.1.1.22 hydroxybutyrate-dimer hydrolase
EC 3.1.1.23 acylglycerol lipase
EC 3.1.1.24 3-oxoadipate enol-lactonase
EC 3.1.1.25 1,4-lactonase
EC 3.1.1.26 galactolipase
EC 3.1.1.27 4-pyridoxolactonase
EC 3.1.1.28 acylearnitine hydrolase
EC 3.1.1.29 aminoacyl-tRNA hydrolase
EC 3.1.1.30 D-arabinonolactonase
EC 3.1.1.31 6-phosphogluconolactonase
EC 3.1.1.32 phospholipase A₁
EC 3.1.1.33 6-acetylglucose deacetylase
EC 3.1.1.34 lipoprotein lipase
EC 3.1.1.35 dihydrocoumarin hydrolase
EC 3.1.1.36 limonin-D-ring-lactonase
EC 3.1.1.37 steroid-lactonase
EC 3.1.1.38 triacetate-lactonase
EC 3.1.1.39 actinomycin lactonase
EC 3.1.1.40 orsellinate-depside hydrolase
EC 3.1.1.41 cephalosporin-C deacetylase
EC 3.1.1.42 chlorogenate hydrolase
EC 3.1.1.43 α-amino-acid esterase
EC 3.1.1.44 4-methylxaloacetate esterase
EC 3.1.1.45 carboxymethylenbutenolidase
EC 3.1.1.46 deoxylimonate A-ring-lactonase
EC 3.1.1.47 1-alkyl-2-acetylglucosynopophosphocholine esterase
EC 3.1.1.48 fusarirnine-C ornithinesterase
EC 3.1.1.49 sinapine esterase
EC 3.1.1.50 wax-ester hydrolase
EC 3.1.1.51 phorbol-diecste hydrolase
EC 3.1.1.52 phosphatidylinositol deacylase
EC 3.1.1.53 stialate O-acetylerase
EC 3.1.1.54 acetoxybutylbithiophene deacetylase
EC 3.1.1.55 acetylsaliclylate deacetylase
EC 3.1.1.56 methylumbelliferyl-acetate deacetylase
EC 3.1.1.57 2-pyrene-4,6-dicarboxylate lactonase
EC 3.1.1.58 N-acetylgalactosaminoglycan deacetylase
EC 3.1.1.59 juvenile-hormone esterase
EC 3.1.1.60 bis(2-ethylhexyl)phthalate esterse
EC 3.1.1.61 protein-glutamate methylesterase
EC 3.1.1.62 now EC 3.5.1.47
EC 3.1.1.63 11-cis-retinyl-palmitate hydrolase
EC 3.1.1.64 all-trans-retinyl-palmitate hydrolase
EC 3.1.1.65 L-rhamnono-1,4-lactonase
EC 3.1.1.66 5-(3,4-diacetoxybut-1-ynyl)-2,2'-bithiophene deacetylase
EC 3.1.1.67 fatty-acetyl-ethyl-ester synthase
EC 3.1.1.68 xylono-1,4-lactonase
EC 3.1.1.69 now EC 3.5.1.89
EC 3.1.1.70 cetaxate benzylesterase
EC 3.1.1.71 acetylalkylglycerol acetylhydrolase
EC 3.1.1.72 acetylyxylan esterase
EC 3.1.1.73 feruloyl esterase
EC 3.1.1.74 cutinase
EC 3.1.1.75 poly(3-hydroxybutyrate) depolymerase
EC 3.1.1.76 poly(3-hydroxyoctanoate) depolymerase
EC 3.1.1.77 acyloxyacyl hydrolase
EC 3.1.1.78 polyneuridine-aldehyde esterase
EC 3.1.1.79 hormone-sensitive lipase
EC 3.1.1.80 acetylajmaline esterase

EC 3.1.2 Thioester Hydrolases

EC 3.1.2.1 acetyl-CoA hydrolase
EC 3.1.2.2 palmitoyl-CoA hydrolase
EC 3.1.2.3 succinyl-CoA hydrolase
EC 3.1.2.4 3-hydroxyisobutyryl-CoA hydrolase
EC 3.1.2.5 hydroxymethylglutaryl-CoA hydrolase
EC 3.1.2.6 hydroxyacylglutathione hydrolase
EC 3.1.2.7 glutathione thiolesterase
EC 3.1.2.8 deleted, included in EC 3.1.2.6
EC 3.1.2.9 deleted
EC 3.1.2.10 formyl-CoA hydrolase
EC 3.1.2.11 acetoacetyl-CoA hydrolase
EC 3.1.2.12 S-formylglutathione hydrolase
EC 3.1.2.13 S-succinylglutathione hydrolase
EC 3.1.2.14 oleoyl-[acyl-carrier-protein] hydrolase
EC 3.1.2.15 ubiquitin thiolesterase
EC 3.1.2.16 citrate lyase deacetylase
EC 3.1.2.17 (S)-methylmalonyl-CoA hydrolase

SUBSTITUTE SHEET (RULE 26)
EC 3.1.2.18 ADP-dependent short-chain-acyl-CoA hydrolase
EC 3.1.2.19 ADP-dependent medium-chain-acyl-CoA hydrolase
EC 3.1.2.20 acyl-CoA hydrolase
EC 3.1.2.21 dodecanoyl-[acyl-carrier protein] hydrolase
EC 3.1.2.22 palmitoyl[protein] hydrolase
EC 3.1.2.23 4-hydroxybenzoyl-CoA thioesterase
EC 3.1.2.24 transferred entry now EC 3.13.1.3
EC 3.1.2.25 phenylacetyl-CoA hydrolase
EC 3.1.2.26 bile-acid-CoA hydrolase
EC 3.1.2.27 choloyl-CoA hydrolase

EC 3.1.3 Phosphoric Monoester Hydrolases

EC 3.1.3.1 alkaline phosphatase
EC 3.1.3.2 acid phosphatase
EC 3.1.3.3 phosphoserine phosphatase
EC 3.1.3.4 phosphatidate phosphatase
EC 3.1.3.5 5'-nucleotidase
EC 3.1.3.6 3'-nucleotidase
EC 3.1.3.7 3'(2'),5'-bisphosphate nucleotidase
EC 3.1.3.8 3-phytase
EC 3.1.3.9 glucose-6-phosphatase
EC 3.1.3.10 glucose-1-phosphatase
EC 3.1.3.11 fructose-bisphosphatase
EC 3.1.3.12 trehalose-phosphatase
EC 3.1.3.13 bisphosphoglycerate phosphatase
EC 3.1.3.14 methylphosphothioglycerate phosphatase
EC 3.1.3.15 histidinol-phosphatase
EC 3.1.3.16 phosphoprotein phosphatase
EC 3.1.3.17 [phosphorylasc] phosphatase
EC 3.1.3.18 phosphoglycolate phosphatase
EC 3.1.3.19 glycerol-2-phosphatase
EC 3.1.3.20 phosphoglycerate phosphatase
EC 3.1.3.21 glycerol-1-phosphatase
EC 3.1.3.22 mannitol-1-phosphatase
EC 3.1.3.23 sugar-phosphatase
EC 3.1.3.24 sucrose-phosphatase
EC 3.1.3.25 inositol-phosphate phosphatase
EC 3.1.3.26 4-phytase
EC 3.1.3.27 phosphatidylglycerophosphatase
EC 3.1.3.28 ADPphosphoglycerate phosphatase
EC 3.1.3.29 N-acylneuraminate-9-phosphatase
EC 3.1.3.30 deleted, included in EC 3.1.3.31
EC 3.1.3.31 nucleotidase
EC 3.1.3.32 polyribonucleotide 3'-phosphatase
EC 3.1.3.33 polyribonucleotide 5'-phosphatase
EC 3.1.3.34 deoxyribonucleotide 3'-phosphatase
EC 3.1.3.35 thymidylate 5'-phosphatase
EC 3.1.3.36 phoshoinositiode 5-phosphatase
EC 3.1.3.37 sedoheptulose-bisphosphatase
EC 3.1.3.38 3-phosphoglycerate phosphatase
EC 3.1.3.39 streptomycin-6-phosphatase
EC 3.1.3.40 guanidino-5-carboxylate-inositol-4-phosphatase
EC 3.1.3.41 4-nitrophenylphosphatase
EC 3.1.3.42 [glycogen-synthase-D] phosphatase
FC 3.1.3.43 [pyruvate dehydrogenase (acetyl-transferring)]-phosphatase
EC 3.1.3.44 [acyl-CoA carboxylase]-phosphatase
FC 3.1.3.45 3-deoxy-\textit{manno}-octulosonate-8-phosphatase
EC 3.1.3.46 fructose-2,6-bisphosphate 2-phosphatase
FC 3.1.3.47 [hydroxymethylglutaryl-CoA reductase (NADPH)]-phosphatase
EC 3.1.3.48 protein-tyrosine-phosphatase
EC 3.1.3.49 [pyruvate kinase]-phosphatase
FC 3.1.3.50 sorbitol-6-phosphatase
EC 3.1.3.51 dolichyl-phosphatase
EC 3.1.3.52 [3-methyl-2-oxobutanoate dehydrogenase (2-methylpropanoyl-transferring)]-phosphatase
EC 3.1.3.53 [myosin-light-chain] phosphatase
EC 3.1.3.54 fructose-2,6-bisphosphate 6-phosphatase
EC 3.1.3.55 caldesmon-phosphatase
EC 3.1.3.56 inositol-polyphosphate 5-phosphatase
EC 3.1.3.57 inositol-1,4-bisphosphate 1-phosphatase
EC 3.1.3.58 sugar-terminal-phosphatase
EC 3.1.3.59 alkylacylgllycerophosphatase
EC 3.1.3.60 phosphoenolpyruvate phosphatase
EC 3.1.3.61 deleted
EC 3.1.3.62 multiple inositol-polyphosphate phosphatase
EC 3.1.3.63 2-carboxy-D-arabinitol-1-phosphatase
EC 3.1.3.64 phosphatidylinositol-3-phosphatase
EC 3.1.3.65 now with FC 3.1.3.64
EC 3.1.3.66 phosphatidylinositol-3,4-bisphosphate 4-phosphatase
EC 3.1.3.67 phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase
EC 3.1.3.68 2-deoxyglucose-6-phosphatase
EC 3.1.3.69 glucosylglycerol 3-phosphatase
EC 3.1.3.70 mannosyl-3-phosphoglycerate phosphatase
EC 3.1.3.71 2-phosphosulfolactate phosphatase
EC 3.1.3.72 5-phytase
EC 3.1.3.73 α-ribazole phosphatase
EC 3.1.3.74 pyridoxal phosphatase
EC 3.1.3.75 phosphothanolamine/phosphocholine phosphatase
EC 3.1.3.76 lipid-phosphate phosphatase
EC 3.1.3.77 acireductone synthase

FC 3.1.4 Phosphoric Diester Hydrolases

EC 3.1.4.1 phosphodiesterase I
EC 3.1.4.2 glycerophosphocholine phosphodiesterase
EC 3.1.4.3 phospholipase C
EC 3.1.4.4 phospholipase D
EC 3.1.4.5 now EC 3.1.21.1
EC 3.1.4.6 now EC 3.1.22.1
EC 3.1.4.7 now EC 3.1.31.1
EC 3.1.4.8 now EC 3.1.27.3
EC 3.1.4.9 now EC 3.1.30.2
EC 3.1.4.10 now EC 4.6.1.13
EC 3.1.4.11 phosphomonoester phospholipase C
EC 3.1.4.12 sphingomyelin phosphodiesterase
EC 3.1.4.13 serine-ethanolaminephosphate phosphodiesterase
EC 3.1.4.14 [acyl-carrier-protein] phosphodiesterase
EC 3.1.4.15 adenyl-[glutamate—ammonia ligase] hydrolase
EC 3.1.4.16 2',3'-cyclic-nucleotide 2'-phosphodiesterase
EC 3.1.4.17 3',5'-cyclic-nucleotide phosphodiesterase
EC 3.1.4.18 now EC 3.1.16.1
EC 3.1.4.19 now EC 3.1.13.3
EC 3.1.4.20 now EC 3.1.13.1
EC 3.1.4.21 now EC 3.1.30.1
EC 3.1.4.22 now EC 3.1.27.5
EC 3.1.4.23 now EC 3.1.27.1
EC 3.1.4.24 deleted
EC 3.1.4.25 now EC 3.1.11.1
EC 3.1.4.26 deleted
EC 3.1.4.27 now EC 3.1.11.2
EC 3.1.4.28 now EC 3.1.11.3
EC 3.1.4.29 deleted
EC 3.1.4.30 now EC 3.1.21.2
EC 3.1.4.31 now EC 3.1.11.4
EC 3.1.4.32 deleted
EC 3.1.4.33 deleted
EC 3.1.4.34 deleted
EC 3.1.4.35 3',5'-cyclic-GMP phosphodiesterase
EC 3.1.4.36 now with EC 3.1.4.43
EC 3.1.4.37 2',3'-cyclic-nucleotide 3'-phosphodiesterase
EC 3.1.4.38 glycerophosphocholine cholinesterase
EC 3.1.4.39 alkylglycerophosphoethanolamine phosphodiesterase
EC 3.1.4.40 CMP-N-acylneuraminic phosphodiesterase
EC 3.1.4.41 sphingomyelin phosphodiesterase D
EC 3.1.4.42 glycerol-1,2-cyclic-phosphate 2-phosphodiesterase
EC 3.1.4.43 glycerophosphoinositol inositolphosphodiesterase
EC 3.1.4.44 glycerophosphoinositol glycerophosphodiesterase
EC 3.1.4.45 N-acetylgalactosamine-1-phosphodiester α-N-acetylgalactosaminidase
EC 3.1.4.46 glycerophosphodiester phosphodiesterase
EC 3.1.4.47 now EC 4.6.1.14
EC 3.1.4.48 dolichylphosphate-glucose phosphodiesterase
EC 3.1.4.49 dolichylphosphate-mannose phosphodiesterase
EC 3.1.4.50 glycosylphosphatidylinositol phospholipase D
EC 3.1.4.51 glucose-1-phospho-D-mannosylglycoprotein phosphodiesterase

EC 3.1.5 Triphosphoric Monoester Hydrolases

EC 3.1.5.1 dGTPase

EC 3.1.6 Sulfuric Ester Hydrolases

EC 3.1.6.1 arylsulfatase
EC 3.1.6.2 steryl-sulfatase
EC 3.1.6.3 glycosulfatase
EC 3.1.6.4 N-acetylgalactosamine-6-sulfatase
EC 3.1.6.5 deleted
EC 3.1.6.6 choline-sulfatase
EC 3.1.6.7 cellulose-polysulfatase
EC 3.1.6.8 cerebroside-sulfatase
EC 3.1.6.9 chondro-4-sulfatase
EC 3.1.6.10 chondro-6-sulfatase
EC 3.1.6.11 disulfoglucosamine-6-sulfatase
EC 3.1.6.12 N-acetylgalactosamine-4-sulfatase
EC 3.1.6.13 iduronate-2-sulfatase
EC 3.1.6.14 N-acetylglucosamine-6-sulfatase
EC 3.1.6.15 N-sulfoglucosamine-3-sulfatase
EC 3.1.6.16 monomethyl-sulfatase
EC 3.1.6.17 D-lactate-2-sulfatase
EC 3.1.6.18 glucuronate-2-sulfatase

EC 3.1.7 Diphosphoric Monoester Hydrolases

EC 3.1.7.1 prenyl-diphosphatase
EC 3.1.7.2 guanosine-3',5'-bis(diphosphate) 3'-diphosphatase
EC 3.1.7.3 monoterpenyl-diphosphatase

EC 3.1.8 Phosphoric Triester Hydrolases

EC 3.1.8.1 aryldialkyl/phosphatase
EC 3.1.8.2 diisopropyl-fluorophosphatase

EC 3.1.11 Exodeoxyribonucleases Producing 5'-Phosphomonoesters

EC 3.1.11.1 exodeoxyribonuclease I
EC 3.1.11.2 exodeoxyribonuclease III
EC 3.1.11.3 exodeoxyribonuclease (lambda-induced)
EC 3.1.11.4 exodeoxyribonuclease (phage SP3-induced)
EC 3.1.11.5 exodeoxyribonuclease V
EC 3.1.11.6 exodeoxyribonuclease VII

EC 3.1.13 Exoribonucleases Producing 5'-Phosphomonoesters

EC 3.1.13.1 exoribonuclease II
EC 3.1.13.2 exoribonuclease H
EC 3.1.13.3 oligonucleotidase
EC 3.1.13.4 poly(A)-specific ribonuclease
EC 3.1.13.5 ribonuclease D

EC 3.1.14 Exoribonucleases Producing 3'-Phosphomonoesters

EC 3.1.14.1 yeast ribonuclease

EC 3.1.15 Exonucleases Active with either Ribo- or Deoxyribonucleic Acids and Producing 5'-Phosphomonoesters

EC 3.1.15.1 venom exonuclease

EC 3.1.16 Exonucleases Active with either Ribo- or Deoxyribonucleic Acids and Producing 3'-Phosphomonoesters

EC 3.1.16.1 spleen exonuclease

EC 3.1.21 Endodeoxyribonucleases Producing 5'-Phosphomonoesters

EC 3.1.21.1 deoxyribonuclease I
EC 3.1.21.2 deoxyribonuclease IV (phage-T7-induced)
EC 3.1.21.3 type I site-specific deoxyribonuclease
EC 3.1.21.4 type II site-specific deoxyribonuclease
EC 3.1.21.5 type III site-specific deoxyribonuclease
EC 3.1.21.6 CC-preferring endodeoxyribonuclease
EC 3.1.21.7 deoxyribonuclease V

EC 3.1.22 Endodeoxyribonucleases Producing 3'-Phosphomonoesters

EC 3.1.22.1 deoxyribonuclease II
EC 3.1.22.2 Aspergillus deoxyribonuclease K
EC 3.1.22.3 now EC 3.1.21.7
EC 3.1.22.4 crossover junction endodeoxyribonuclease
EC 3.1.22.5 deoxyribonuclease X

EC 3.1.23 and EC 3.1.24 now EC 3.1.21.3, EC 3.1.21.4 and EC 3.1.21.5

EC 3.1.25 Site-Specific Endodeoxyribonucleases Specific for Altered Bases

EC 3.1.25.1 deoxyribonuclease (pyrimidine dimer)
EC 3.1.25.2 now EC 4.2.99.18

EC 3.1.26 Endoribonucleases Producing 5'-Phosphomonoesters

EC 3.1.26.1 Physarum polycephalum ribonuclease
EC 3.1.26.2 ribonuclease alpha
EC 3.1.26.3 ribonuclease III
EC 3.1.26.4 calf thymus ribonuclease H
EC 3.1.26.5 ribonuclease P
EC 3.1.26.6 ribonuclease IV
EC 3.1.26.7 ribonuclease P4
EC 3.1.26.8 ribonuclease M5
EC 3.1.26.9 ribonuclease [poly-(U)-specific]
EC 3.1.26.10 ribonuclease IX
EC 3.1.26.11 tRNase Z

EC 3.1.27 Endoribonucleases Producing 3'-Phosphomonoesters

EC 3.1.27.1 ribonuclease T2
EC 3.1.27.2 Bacillus subtilis ribonuclease
EC 3.1.27.3 ribonuclease T1
EC 3.1.27.4 ribonuclease U2
EC 3.1.27.5 pancreatic ribonuclease
EC 3.1.27.6 Enterobacter ribonuclease
EC 3.1.27.7 ribonuclease F
EC 3.1.27.8 ribonuclease V
EC 3.1.27.9 tRNA-intron endonuclease
EC 3.1.27.10 rRNA endonuclease

EC 3.1.30 Endoribonucleases Active with either Ribo- or Deoxyribonucleic Acids and Producing 5'-Phosphomonoesters

EC 3.1.30.1 Aspergillus nuclease S1
EC 3.1.30.2 Serratia marcescens nuclease
EC 3.1.31 Endoribonucleases Active with either Ribo- or Deoxyribonucleic Acids and Producing 3'-Phosphomonoesters

EC 3.1.31.1 micrococcal nuclease

EC 3.2 Glycosylases

EC 3.2.1 Glycosidases, i.e. enzymes hydrolysing O- and S-glycosyl compounds

EC 3.2.1.1 α-amylase
EC 3.2.1.2 β-amylase
EC 3.2.1.3 glucan 1,4-α-glucosidase
EC 3.2.1.4 cellulase
EC 3.2.1.5 deleted
EC 3.2.1.6 endo-1,3(4)-β-glucanase
EC 3.2.1.7 mannanase
EC 3.2.1.8 endo-1,4-β-xylanase
EC 3.2.1.9 deleted
EC 3.2.1.10 oligo-1,6-glucosidase
EC 3.2.1.11 dextranase
EC 3.2.1.12 deleted, included in EC 3.2.1.54
EC 3.2.1.13 deleted, included in EC 3.2.1.54
EC 3.2.1.14 chitinase
EC 3.2.1.15 polygalacturonase
EC 3.2.1.16 deleted
EC 3.2.1.17 lysozyme
EC 3.2.1.18 exo-α-d-galactosidase
EC 3.2.1.19 deleted
EC 3.2.1.20 α-glucosidase
EC 3.2.1.21 β-glucosidase
EC 3.2.1.22 α-galactosidase
EC 3.2.1.23 β-galactosidase
EC 3.2.1.24 α-mannosidase
EC 3.2.1.25 β-mannosidase
EC 3.2.1.26 β-fructofuranosidase
EC 3.2.1.27 deleted
EC 3.2.1.28 α,α-trehalase
EC 3.2.1.29 deleted, included in EC 3.2.1.52
EC 3.2.1.30 deleted, included in EC 3.2.1.52
EC 3.2.1.31 β-glucuronidase
EC 3.2.1.32 xylan endo-1,3-β-xylanase
EC 3.2.1.33 amylo-1,6-glucosidase
EC 3.2.1.34 deleted, included in EC 3.2.1.35
EC 3.2.1.35 hyaluronoglucosaminidase
EC 3.2.1.36 hyaluronoglucuronidase
EC 3.2.1.37 xylan 1,4-β-xylanase
EC 3.2.1.38 β-D-fucosidase
EC 3.2.1.39 glucan endo-1,3-β-D-glucosidase
EC 3.2.1.40 α-L-rhamnosidase
EC 3.2.1.41 pullulanase
EC 3.2.1.42 GDP-glucosidase
EC 3.2.1.43 β-L-rhamnosidase
EC 3.2.1.44 fucoidanase
EC 3.2.1.45 glucosylceramidase
EC 3.2.1.46 galactosylceramidase
EC 3.2.1.47 galactosylgalactosylglucosylceramidase
EC 3.2.1.48 sucrose α-glucosidase
EC 3.2.1.49 α-N-acetylgalactosaminidase
EC 3.2.1.50 α-N-acetylglucosaminidase
EC 3.2.1.51 α-L-fucosidase
EC 3.2.1.52 β-L-N-acetylhexosaminidase
EC 3.2.1.53 β-N-acetylgalactosaminidase
EC 3.2.1.54 cyclomaltooligosaccharide
EC 3.2.1.55 α-N-arabinofuranosidase
EC 3.2.1.56 glucuronosyl-disulfoglucosamine glucuronidase
EC 3.2.1.57 isopullulanase
EC 3.2.1.58 glucan 1,3-β-glucosidase
EC 3.2.1.59 glucan endo-1,3-α-glucosidase
EC 3.2.1.60 glucan 1,4-α-maltotetrahydrolase
EC 3.2.1.61 mycodextranase
EC 3.2.1.62 glycosylceramidase
EC 3.2.1.63 1,2-α-L-fucosidase
EC 3.2.1.64 2,6-β-fructan 6-levanbiohydrolase
EC 3.2.1.65 levanase
EC 3.2.1.66 quercitrinase
EC 3.2.1.67 galacturan 1,4-α-galacturonidase
EC 3.2.1.68 isoamylase
EC 3.2.1.69 deleted, included in EC 3.2.1.41
EC 3.2.1.70 glucan 1,6-α-glucosidase
EC 3.2.1.71 glucan endo-1,2-β-glucosidase
EC 3.2.1.72 xylan 1,3-β-xylanase
EC 3.2.1.73 lichenase
EC 3.2.1.74 glucan 1,4-β-glucosidase
EC 3.2.1.75 glucan endo-1,6-β-glucosidase
EC 3.2.1.76 L-iduronidase
EC 3.2.1.77 mannan 1,2-(1,3)-α-mannosidase
EC 3.2.1.78 mannan endo-1,4-β-mannosidase
EC 3.2.1.79 deleted, included in EC 3.2.1.55
EC 3.2.1.80 fructan β-fructosidase
EC 3.2.1.81 β-agarase
EC 3.2.1.82 exo-poly-α-galacturonidosidase
EC 3.2.1.83 κ-carrageenase
EC 3.2.1.84 glucan 1,3-α-glucosidase
EC 3.2.1.85 6-phospho-β-galactosidase
EC 3.2.1.86 6-phospho-β-glucosidase
EC 3.2.1.87 capsular polysaccharide endo-1,3-α-galactosidase
EC 3.2.1.88 β-L-arabinosidase
EC 3.2.1.89 arabinogalactan endo-1,4-β-galactosidase
EC 3.2.1.90 deleted, not sufficiently characterised.
EC 3.2.1.91 cellulose 1,4-β-cellubiosidase
EC 3.2.1.92 peptidoglycan β-N-acetylglucosaminidase
EC 3.2.1.93 α,β-phosphotrehalase
EC 3.2.1.94 glucan 1,6-α-isomaltosidase
EC 3.2.1.95 dextran 1,6-α-isomaltotriosidase
EC 3.2.1.96 mannosyl-glycoprotein endo-β-N-acetylglucosaminidase
EC 3.2.1.97 glycopeptide α-N-acetylglucosaminidase
EC 3.2.1.98 glucan 1,4-α-maltodextranase
EC 3.2.1.99 arabinan endo-1,5-α-L-arabinosidase
EC 3.2.1.100 mannan 1,4-mannobiosidase
EC 3.2.1.101 mannan endo-1,6-α-mannosidase
EC 3.2.1.102 blood-group-substance endo-1,4-β-galactosidase
EC 3.2.1.103 keratan-sulfate endo-1,4-β-galactosidase
EC 3.2.1.104 steryl-β-glucosidase
EC 3.2.1.105 strictosidine β-glucosidase
EC 3.2.1.106 mannosyl-oligosaccharide glucosidase
EC 3.2.1.107 protein-glucosylgalactosylhydroxylysine glucosidase
EC 3.2.1.108 lactase
EC 3.2.1.109 endogalactosaminidase
EC 3.2.1.110 mucinaminylserine mucinaminidase
EC 3.2.1.111 1,3-α-L-fucosidase
EC 3.2.1.112 2-deoxyglucosidase
EC 3.2.1.113 mannosyl-oligosaccharide 1,2-α-mannosidase
EC 3.2.1.114 mannosyl-oligosaccharide 1,3-1,6-α-mannosidase
EC 3.2.1.115 branched-dextran exo-1,2-α-glucosidase
EC 3.2.1.116 glucan 1,4-α-maltotrihydrolase
EC 3.2.1.117 amygdalin β-glucosidase
EC 3.2.1.118 prunasin β-glucosidase
EC 3.2.1.119 vicitan β-glucosidase
EC 3.2.1.120 oligoxyloglucan β-glucosidase
EC 3.2.1.121 polymannuronate hydrolase
EC 3.2.1.122 maltose-6'-phosphate glucosidase
EC 3.2.1.123 endoglycosylceramidase
EC 3.2.1.124 3-deoxy-2-octulosonidase
EC 3.2.1.125 raucaffricine β-glucosidase
EC 3.2.1.126 coniferin β-glucosidase
EC 3.2.1.127 1,6-α-L-fucosidase
EC 3.2.1.128 glycyrrhizinate β-glucuronidase
EC 3.2.1.129 endo-α-sialidase
EC 3.2.1.130 glycophosphatidylendo-α-1,2-mannosidase
EC 3.2.1.131 xylan α-1,2-glucuronosidase
EC 3.2.1.132 chitosanase
EC 3.2.1.133 glucan 1,4-α-maltotrihydrolase
EC 3.2.1.134 difructose-anhydride synthase
EC 3.2.1.135 neopullulanase
EC 3.2.1.136 glucuronoxarabinofuranosyl endo-1,4-β-xylanase
EC 3.2.1.137 mannan exo-1,2,1,6-α-mannosidase
EC 3.2.1.138 now EC 4.2.2.15
EC 3.2.1.139 α-glucuronidase
EC 3.2.1.140 lacto-N-biosidase
EC 3.2.1.141 4-α-D-[(1→4)-α-D-glucano] trehalose trehalohydrolase
EC 3.2.1.142 limit dextrinase
EC 3.2.1.143 poly(ADP-ribose) glycohydrolase
EC 3.2.1.144 3-deoxyoctulosonase
EC 3.2.1.145 galactan 1,3-β-galactosidase
EC 3.2.1.146 β-galactofuranosidase
EC 3.2.1.147 thioglucohydrolase
EC 3.2.1.148 now EC 4.4.1.21
EC 3.2.1.149 β-primeverosidase
EC 3.2.1.150 oligoxyloglucan reducing-end-specific cellbiohydrolase
EC 3.2.1.151 xyloglucan-specific endo-β-1,4-glucanase
EC 3.2.1.152 mannosylglycoprotein endo-β-mannosidase
EC 3.2.1.153 fructan β-(2,1)-fructosidase
EC 3.2.1.154 fructan β-(2,6)-fructosidase
EC 3.2.1.155 xyloglucan-specific exo-β-1,4-glucanase
EC 3.2.1.156 oligosaccharide reducing-end xylanase
EC 3.2.1.157 t-carrageenase
EC 3.2.1.158 α-agarase
EC 3.2.1.159 α-neoagaro-oligosaccharide hydrolase
EC 3.2.1.155
EC 3.2.1.161 β-apiosyl-β-glucosidase

**EC 3.2.2 Hydrolysing N-Glycosyl Compounds**

EC 3.2.2.1 purine nucleosidase
EC 3.2.2.2 inosine nucleosidase
EC 3.2.2.3 uridine nucleosidase
EC 3.2.2.4 AMP nucleosidase
EC 3.2.2.5 NAD⁺ nucleosidase
EC 3.2.2.6 NAD(P)⁺ nucleosidase
EC 3.2.2.7 adenosine nucleosidase
EC 3.2.2.8 ribosylpyrimidine nucleosidase
EC 3.2.2.9 adenosylhomocysteine nucleosidase
EC 3.2.2.10 pyrimidine-5'-nucleotidase nucleosidase
EC 3.2.2.11 β-aspartyl-N-acetylglucosaminidase
EC 3.2.2.12 inosinate nucleosidase
EC 3.2.2.13 1-methyladenosine nucleosidase
EC 3.2.2.14 NMN nucleosidase
EC 3.2.2.15 DNA-deoxyinosine glycosylase
EC 3.2.2.16 methylthioadenosine nucleosidase
EC 3.2.2.17 deoxyribosylpyrimidine endonucleosidase
EC 3.2.2.18 deleted, included in EC 3.5.1.52
EC 3.2.2.19 ADP-ribosylarginine hydrolase
EC 3.2.2.20 DNA-3-methyladenine glycosylase I
EC 3.2.2.21 DNA-3-methyladenine glycosylase II
EC 3.2.2.22 rRNA N-glycosylase
EC 3.2.2.23 DNA-formamidopyrimidine glycosylase
EC 3.2.2.24 ADP-ribosyl-[dinitrogen reductase] hydrolase

**EC 3.2.3 Hydrolysing S-Glycosyl Compounds** (discontinued)

EC 3.2.3.1 now EC 3.2.1.147

EC 3.3 Acting on Ether Bonds

**EC 3.3.1 Thioether and Trialkylsulfonium Hydrolases**

EC 3.3.1.1 adenosylhomocysteinase
EC 3.3.1.2 adenosylmethionine hydrolase
EC 3.3.1.3 now EC 3.2.1.148

**EC 3.3.2 Ether Hydrolases**

EC 3.3.2.1 isochorismatase
EC 3.3.2.2 alkenylglycerophosphocholine hydrolase
EC 3.3.2.3 now EC 3.3.2.9 and EC 3.3.2.10
EC 3.3.2.4 trans-epoxysuccinate hydrolase
EC 3.3.2.5 alkenylglycerophosphoethanolamine hydrolase
EC 3.3.2.6 leukotriene-Α₄ hydrolase
EC 3.3.2.7 hepxilin-epoxide hydrolase
EC 3.3.2.8 limonene-1,2-epoxide hydrolase

EC 3.3.2.9 microsomal epoxide hydrolase
EC 3.3.2.10 soluble epoxide hydrolase
EC 3.3.2.11 cholesterol-5,6-oxide hydrolase

EC 3.4 Acting on peptide bonds (Peptidases)

EC 3.4.1.1 now EC 3.4.11.1
EC 3.4.1.2 now EC 3.4.11.2
EC 3.4.1.3 now EC 3.4.11.4
EC 3.4.1.4 now EC 3.4.11.5
EC 3.4.2.1 now EC 3.4.17.1
EC 3.4.2.2 now EC 3.4.17.2
EC 3.4.2.3 now EC 3.4.17.4
EC 3.4.3.1 now EC 3.4.13.18
EC 3.4.3.2 now EC 3.4.13.18
EC 3.4.3.3 now EC 3.4.13.3
EC 3.4.3.4 now EC 3.4.13.5
EC 3.4.3.5 now EC 3.4.13.6
EC 3.4.3.6 now EC 3.4.13.8
EC 3.4.3.7 now EC 3.4.13.9
EC 3.4.4.1 now EC 3.4.23.1
EC 3.4.4.2 now EC 3.4.23.2
EC 3.4.4.3 now EC 3.4.23.4
EC 3.4.4.4 now EC 3.4.21.4
EC 3.4.4.5 now EC 3.4.21.1
EC 3.4.4.6 now EC 3.4.21.1
EC 3.4.4.7 now covered by EC 3.4.21.36, EC 3.4.21.37
EC 3.4.4.8 now EC 3.4.21.9
EC 3.4.4.9 now EC 3.4.14.1
EC 3.4.4.10 now EC 3.4.22.2
EC 3.4.4.11 now EC 3.4.22.6
EC 3.4.4.12 now EC 3.4.22.3
EC 3.4.4.13 now EC 3.4.21.5
EC 3.4.4.14 now EC 3.4.21.7
EC 3.4.4.15 now EC 3.4.23.15
EC 3.4.4.16 now covered by EC 3.4.21.62 to EC 3.4.21.67
EC 3.4.4.17 now covered by EC 3.4.23.20 to EC 3.4.23.30
EC 3.4.4.18 now EC 3.4.22.10
EC 3.4.4.19 now EC 3.4.24.3
EC 3.4.4.20 now EC 3.4.22.8
EC 3.4.4.21 now EC 3.4.21.34
EC 3.4.4.22 now EC 3.4.23.3
EC 3.4.4.23 now EC 3.4.23.5
EC 3.4.4.24 now covered by EC 3.4.22.32, EC 3.4.22.33
EC 3.4.4.25 deleted

EC 3.4.11 Aminopeptidases

EC 3.4.11.1 leucyl aminopeptidase
EC 3.4.11.2 membrane alanyl aminopeptidase
EC 3.4.11.3 cystinyl aminopeptidase
EC 3.4.11.4 tripeptide aminopeptidase
EC 3.4.11.5 prolyl aminopeptidase
EC 3.4.11.6 arginyl aminopeptidase
EC 3.4.11.7 glutamyl aminopeptidase
EC 3.4.11.8 now EC 3.4.19.3
EC 3.4.11.9 Xaa-Pro aminopeptidase
EC 3.4.11.10 bacterial leucyl aminopeptidase
EC 3.4.11.11 deleted
EC 3.4.11.12 deleted (supplement 4)
EC 3.4.11.13 clostridial aminopeptidase
EC 3.4.11.14 cytosol alanyl aminopeptidase
EC 3.4.11.15 lysyl aminopeptidase
EC 3.4.11.16 Xaa-Trp aminopeptidase
EC 3.4.11.17 tryptophanyl aminopeptidase
EC 3.4.11.18 methionyl aminopeptidase
EC 3.4.11.19 D-stereospecific aminopeptidase
EC 3.4.11.20 aminopeptidase Ey
EC 3.4.11.21 aspartyl aminopeptidase
EC 3.4.11.22 aminopeptidase I
EC 3.4.11.23 pepB aminopeptidase
EC 3.4.12.1 now EC 3.4.16.1
EC 3.4.12.2 now EC 3.4.17.1
EC 3.4.12.3 now EC 3.4.17.2
EC 3.4.12.4 now EC 3.4.16.2
EC 3.4.12.5 now EC 3.4.19.10
EC 3.4.12.6 now EC 3.4.17.8
EC 3.4.12.7 now EC 3.4.17.3
EC 3.4.12.8 now EC 3.4.17.4
EC 3.4.12.9 deleted
EC 3.4.12.10 now EC 3.4.19.9
EC 3.4.12.11 now EC 3.4.17.6
EC 3.4.12.12 now EC 3.4.16.1
EC 3.4.12.13 deleted

EC 3.4.13 Dipeptidases
EC 3.4.13.1 now EC 3.4.13.18
EC 3.4.13.2 now EC 3.4.13.18
EC 3.4.13.3 Xaa-His dipeptidase
EC 3.4.13.4 Xaa-Arg dipeptidase
EC 3.4.13.5 Xaa-Methyl-His dipeptidase
EC 3.4.13.6 now EC 3.4.11.2 (supplement 4)
EC 3.4.13.7 Glu-Glu dipeptidase
EC 3.4.13.8 now EC 3.4.17.21 (supplement 6)
EC 3.4.13.9 Xaa-Pro dipeptidase
EC 3.4.13.10 now EC 3.4.19.5
EC 3.4.13.11 deleted, included in EC 3.4.13.18
EC 3.4.13.12 Met-Xaa dipeptidase
EC 3.4.13.13 deleted, included in EC 3.4.13.3
EC 3.4.13.14 deleted
EC 3.4.13.15 deleted, included in EC 3.4.13.18
EC 3.4.13.16 deleted
EC 3.4.13.17 non-stereospecific dipeptidase
EC 3.4.13.18 cytosol nonspecific dipeptidase
EC 3.4.13.19 membrane dipeptidase
EC 3.4.13.20 β-Ala-His dipeptidase
EC 3.4.13.21 dipeptidase E

EC 3.4.14 Dipeptidyl-peptidases and tripeptidyl-peptidases
EC 3.4.14.1 dipeptidyl-peptidase I
EC 3.4.14.2 dipeptidyl-peptidase II
EC 3.4.14.3 now EC 3.4.19.1
EC 3.4.14.4 dipeptidyl-peptidase III
EC 3.4.14.5 dipeptidyl-peptidase IV
EC 3.4.14.6 dipeptidyl-dipeptidase
EC 3.4.14.7 deleted
EC 3.4.14.8 now covered by EC 3.4.14.9, EC 3.4.14.10
EC 3.4.14.9 tripeptidyl-peptidase I
EC 3.4.14.10 tripeptidyl-peptidase II
EC 3.4.14.11 Xaa-Pro dipeptidyl-peptidase
EC 3.4.14.12 prolyltripeptidyl aminopeptidase

EC 3.4.15 Peptidyl-dipeptidases
EC 3.4.15.1 peptidyl-dipeptidase A
EC 3.4.15.2 now EC 3.4.19.2
EC 3.4.15.3 deleted, included in EC 3.4.15.5 (supplement 2)
EC 3.4.15.4 peptidyl-dipeptidase B
EC 3.4.15.5 peptidyl-dipeptidase Dcp

EC 3.4.16 Serine-type carboxypeptidases
EC 3.4.16.1 deleted, included in EC 3.4.16.5, EC 3.4.16.6 (supplement 1)
EC 3.4.16.2 lysosomal Pro-Xaa carboxypeptidase
EC 3.4.16.3 deleted, included in EC 3.4.16.5 (supplement 1)
EC 3.4.16.4 serine-type D-Ala-D-Ala carboxypeptidase
EC 3.4.16.5 carboxypeptidase C
EC 3.4.16.6 carboxypeptidase D

EC 3.4.17 Metallo carboxypeptidases
EC 3.4.17.1 carboxypeptidase A
EC 3.4.17.2 carboxypeptidase B
EC 3.4.17.3 lysine carboxypeptidase
EC 3.4.17.4 Gly-Xaa carboxypeptidase
EC 3.4.17.5 deleted
EC 3.4.17.6 alanine carboxypeptidase
EC 3.4.17.7 now EC 3.4.19.10
EC 3.4.17.8 muramoylpentapeptide carboxypeptidase
EC 3.4.17.9 deleted, included in EC 3.4.17.4
EC 3.4.17.10 carboxypeptidase E
EC 3.4.17.11 glutamate carboxypeptidase
EC 3.4.17.12 carboxypeptidase M
EC 3.4.17.13 muramoyl tetrapeptide carboxypeptidase
EC 3.4.17.14 zinc D-Ala-D-Ala carboxypeptidase
EC 3.4.17.15 carboxypeptidase A2
EC 3.4.17.16 membrane Pro-Xaa carboxypeptidase
EC 3.4.17.17 tubulinnyl-Tyr carboxypeptidase
EC 3.4.17.18 carboxypeptidase T
EC 3.4.17.19 carboxypeptidase Taq
EC 3.4.17.20 carboxypeptidase U
EC 3.4.17.21 glutamate carboxypeptidase II
EC 3.4.17.22 metallocarboxypeptidase D

**EC 3.4.18 Cysteine-type carboxypeptidases**

EC 3.4.18.1 cathepsin X

**EC 3.4.19 Omega peptidases**

EC 3.4.19.1 acylaminoacyl-peptidase
EC 3.4.19.2 peptidyl-glycinamidase
EC 3.4.19.3 pyroglutamyl-peptidase I
EC 3.4.19.4 deleted
EC 3.4.19.5 β-aspartyl-peptidase
EC 3.4.19.6 pyroglutamyl-peptidase II
EC 3.4.19.7 N-formylmethionyl-peptidase
EC 3.4.19.8 now EC 3.4.17.21 (supplement 6)
EC 3.4.19.9 γ-glutamyl hydrolase
EC 3.4.19.10 now EC 3.5.1.28 (supplement 4)
EC 3.4.19.11 γ-D-Glutamyl-meso-diaminopimelate peptidase I
EC 3.4.19.12 ubiquitinyl hydrolase I

**EC 3.4.21 Serine endopeptidases**

EC 3.4.21.1 chymotrypsin
EC 3.4.21.2 chymotrypsin C
EC 3.4.21.3 metridin
EC 3.4.21.4 trypsin
EC 3.4.21.5 thrombin
EC 3.4.21.6 coagulation Factor Xa
EC 3.4.21.7 plasmin
EC 3.4.21.8 now covered by EC 3.4.21.34, EC 3.4.21.35
EC 3.4.21.9 enteropeptidase
EC 3.4.21.10 acrosin
EC 3.4.21.11 now covered by EC 3.4.21.36, EC 3.4.21.37
EC 3.4.21.12 α-Lytic endopeptidase
EC 3.4.21.13 now EC 3.4.16.1
EC 3.4.21.14 now covered by EC 3.4.21.62 to EC 3.4.21.65, EC 3.4.21.67
EC 3.4.21.15 now EC 3.4.21.63
EC 3.4.21.16 deleted
EC 3.4.21.17 deleted
EC 3.4.21.18 deleted
EC 3.4.21.19 glutamyl endopeptidase
EC 3.4.21.20 cathepsin G
EC 3.4.21.21 coagulation Factor VIIa
EC 3.4.21.22 coagulation Factor IXa
EC 3.4.21.23 deleted
EC 3.4.21.24 deleted
EC 3.4.21.25 cucumisin
EC 3.4.21.26 prolyl oligopeptidase
EC 3.4.21.27 coagulation Factor XIa
EC 3.4.21.28 deleted, included in EC 3.4.21.74
EC 3.4.21.29 deleted, included in EC 3.4.21.74
EC 3.4.21.30 deleted, included in EC 3.4.21.74
EC 3.4.21.31 now covered by EC 3.4.21.68, EC 3.4.21.73
EC 3.4.21.32 brachyurin
EC 3.4.21.33 deleted
EC 3.4.21.34 plasma kallikrein
EC 3.4.21.35 tissue kallikrein
EC 3.4.21.36 pancreatic elastase
EC 3.4.21.37 leukocyte elastase
EC 3.4.21.38 coagulation Factor XIIa
EC 3.4.21.39 chymase
EC 3.4.21.40 deleted
EC 3.4.21.41 complement subcomponent C1r
EC 3.4.21.42 complement subcomponent C1s
EC 3.4.21.43 classical-complement-pathway C3/C5 convertase
EC 3.4.21.44 deleted, included in EC 3.4.21.43
EC 3.4.21.45 complement Factor I
EC 3.4.21.46 complement Factor D
EC 3.4.21.47 alternative-complement-pathway C3/C5 convertase
EC 3.4.21.48 cerevisin
EC 3.4.21.49 hypodermic C
EC 3.4.21.50 lysyl endopeptidase
EC 3.4.21.51 deleted
EC 3.4.21.52 deleted
EC 3.4.21.53 endopeptidase Lα
EC 3.4.21.54 γ-relin
EC 3.4.21.55 Venombin AB
EC 3.4.21.56 deleted
EC 3.4.21.57 leucyl endopeptidase
EC 3.4.21.58 deleted
EC 3.4.21.59 tryptase
EC 3.4.21.60 scutellarin
EC 3.4.21.61 kexin
EC 3.4.21.62 subtilisin
EC 3.4.21.63 oryzin
EC 3.4.21.64 peptidase K
EC 3.4.21.65 thermomycolin
EC 3.4.21.66 thermitase
EC 3.4.21.67 endopeptidase So
EC 3.4.21.68 t-plasminogen activator
EC 3.4.21.69 protein C (activated)
EC 3.4.21.70 pancreatic endopeptidase E
EC 3.4.21.71 pancreatic elastase II
EC 3.4.21.72 IgA-specific serine endopeptidase
EC 3.4.21.73 u-plasminogen activator
EC 3.4.21.74 venombin A
EC 3.4.21.75 furin
EC 3.4.21.76 myeloblastin
EC 3.4.21.77 semenogelase
EC 3.4.21.78 granzyme A
EC 3.4.21.79 granzyme B
EC 3.4.21.80 streptogrispin A
EC 3.4.21.81 streptogrisin B
EC 3.4.21.82 glutamyl endopeptidase II
EC 3.4.21.83 oligopeptidase B
EC 3.4.21.84 limulus clotting factor C
EC 3.4.21.85 limulus clotting factor B
EC 3.4.21.86 limulus clotting enzyme
EC 3.4.21.87 now EC 3.4.23.49
EC 3.4.21.88 repressor LexA
EC 3.4.21.89 signal peptidase I
EC 3.4.21.90 togavirin
EC 3.4.21.91 flavivirin
EC 3.4.21.92 endopeptidase Clp
EC 3.4.21.93 proprotein convertase 1
EC 3.4.21.94 proprotein convertase 2
EC 3.4.21.95 snake venom factor V activator
EC 3.4.21.96 lactocepin
EC 3.4.21.97 assemblin
EC 3.4.21.98 hepacivirin
EC 3.4.21.99 spermosin
EC 3.4.21.100 pseudomonalisin
EC 3.4.21.101 xanthomonalisin
EC 3.4.21.102 C-terminal processing peptidase
EC 3.4.21.103 physarolisin
EC 3.4.21.104 mannan-binding lectin-associated serine protease-2
EC 3.4.21.105 rhomboid protease
EC 3.4.21.106 hepsin
EC 3.4.21.107 peptidase Do
EC 3.4.21.108 HtrA2 peptidase
EC 3.4.21.109 matriptase
EC 3.4.21.110 C5a peptidase
EC 3.4.21.111 aqualysin 1
EC 3.4.21.112 site-1 protease
EC 3.4.21.113 pestivirus NS3 polyprotein peptidase
EC 3.4.21.114 equine arterivirus serine peptidase
EC 3.4.21.115 infectious pancreatic necrosis birnavirus Vp4 peptidase
EC 3.4.21.116 SponV peptidase
EC 3.4.21.117 stratum corneum chymotryptic enzyme
EC 3.4.21.118 kallikrein 8
EC 3.4.21.119 kallikrein 13

EC 3.4.22 Cysteine endopeptidases

EC 3.4.22.1 cathepsin B
EC 3.4.22.2 papain
EC 3.4.22.3 ficain
EC 3.4.22.4 now covered by EC 3.4.22.32, EC 3.4.22.33
EC 3.4.22.5 now EC 3.4.22.33
EC 3.4.22.6 chymopapain
EC 3.4.22.7 asclepian
EC 3.4.22.8 clostripain
EC 3.4.22.9 now EC 3.4.21.48
EC 3.4.22.10 streptopain
EC 3.4.22.11 now EC 3.4.24.56 (supplement 3)
EC 3.4.22.12 now EC 3.4.19.9
EC 3.4.22.13 deleted
EC 3.4.22.14 actinidain
EC 3.4.22.15 cathepsin L
EC 3.4.22.16 cathepsin H
EC 3.4.22.17 now EC 3.4.22.52 and EC 3.4.22.53
EC 3.4.22.18 deleted, included in EC 3.4.21.26
EC 3.4.22.19 deleted, included in EC 3.4.24.15
EC 3.4.22.20 deleted
EC 3.4.22.21 deleted, included in EC 3.4.99.46
EC 3.4.22.22 now EC 3.4.24.37
EC 3.4.22.23 deleted, included in EC 3.4.21.61
EC 3.4.22.24 cathepsin T
EC 3.4.22.25 glycyl endopeptidase
EC 3.4.22.26 cancer procoagulant
EC 3.4.22.27 cathepsin S
EC 3.4.22.28 picornain 3C
EC 3.4.22.29 picornain 2A
EC 3.4.22.30 caricain
EC 3.4.22.31 ananain
EC 3.4.22.32 stem bromelain
EC 3.4.22.33 fruit bromelain
EC 3.4.22.34 legumain
EC 3.4.22.35 histolysain
EC 3.4.22.36 caspase-1
EC 3.4.22.37 gingipain R
EC 3.4.22.38 cathepsin K
EC 3.4.22.39 adenain
EC 3.4.22.40 bleomycin hydrolase
EC 3.4.22.41 cathepsin F
EC 3.4.22.42 cathepsin O
EC 3.4.22.43 cathepsin V
EC 3.4.22.44 nuclear-inclusion-a endopeptidase
EC 3.4.22.45 helper-component proteinase
EC 3.4.22.46 L-peptidase
EC 3.4.22.47 gingipain K
EC 3.4.22.48 staphopain
EC 3.4.22.49 separase
EC 3.4.22.50 V-cath endopeptidase
EC 3.4.22.51 cruzipain
EC 3.4.22.52 calpain-1
EC 3.4.22.53 calpain-2

EC 3.4.23 Aspartic endopeptidases

EC 3.4.23.1 pepsin A
EC 3.4.23.2 pepsin B
EC 3.4.23.3 gastricsin
EC 3.4.23.4 chymosin
EC 3.4.23.5 cathepsin D
EC 3.4.23.6 now covered by EC 3.4.23.18 to EC 3.4.23.28, EC 3.4.23.30
EC 3.4.23.7 now EC 3.4.24.20
EC 3.4.23.8 now EC 3.4.24.25
EC 3.4.23.9 now EC 3.4.24.21
EC 3.4.23.10 now EC 3.4.24.22
EC 3.4.23.11 deleted
EC 3.4.23.12 nepenthesin
EC 3.4.23.13 deleted
EC 3.4.23.14 deleted
EC 3.4.23.15 renin
EC 3.4.23.16 HIV-1 retropepsin
EC 3.4.23.17 Pro-opiomelanocortin converting enzyme
EC 3.4.23.18 aspergillopepsin I
EC 3.4.23.19 aspergillopepsin II
EC 3.4.23.20 penicillopepsin
EC 3.4.23.21 rhizopuspepsin
EC 3.4.23.22 endothiapepsin
EC 3.4.23.23 mucorpepsin
EC 3.4.23.24 candidapepsin
EC 3.4.23.25 Saccharopepsin
EC 3.4.23.26 rhodotorulapepsin
EC 3.4.23.27 now EC 3.4.21.103
EC 3.4.23.28 acrocylindropepsin
EC 3.4.23.29 polyvoropepsin
EC 3.4.23.30 pycnoporepepsin
EC 3.4.23.31 scytalidopepsin A
EC 3.4.23.32 scytalidopepsin B
EC 3.4.23.33 now EC 3.4.21.101
EC 3.4.23.34 cathepsin E
EC 3.4.23.35 barrierpepsin
EC 3.4.23.36 signal peptidase II
EC 3.4.23.37 now EC 3.4.21.100
EC 3.4.23.38 plasmapesin I
EC 3.4.23.39 plasmapesin II
EC 3.4.23.40 phytopespin
EC 3.4.23.41 yapsin 1
EC 3.4.23.42 thermopespin
EC 3.4.23.43 prepin peptidase
EC 3.4.23.44 nodavirus endopeptidase
EC 3.4.23.45 memapsin 1
EC 3.4.23.46 memapsin 2
EC 3.4.23.47 HIV-2 retropepsin
EC 3.4.23.48 plasminogen activator Pla
EC 3.4.23.49 omptin

EC 3.4.24 Metalloendopeptidases

EC 3.4.24.1 atrolysin A
EC 3.4.24.2 deleted
EC 3.4.24.3 microbial collagenase
EC 3.4.24.4 now covered by EC 3.4.24.25 to EC 3.4.24.32, EC 3.4.24.39, EC 3.4.24.40
EC 3.4.24.5 now covered by EC 3.4.22.17, EC 3.4.25.1
EC 3.4.24.6 leucolysin
EC 3.4.24.7 interstitial collagenase
EC 3.4.24.8 deleted, included in EC 3.4.24.3
EC 3.4.24.9 deleted
EC 3.4.24.10 deleted
EC 3.4.24.11 ncprylisin
EC 3.4.24.12 enverylisin
EC 3.4.24.13 IgA-specific metalloendopeptidase
EC 3.4.24.14 procollagen N-endopeptidase
EC 3.4.24.15 thimet oligopeptidase
EC 3.4.24.16 neurolysin
EC 3.4.24.17 stromelysin 1
EC 3.4.24.18 meprin A
EC 3.4.24.19 procollagen C-endopeptidase
EC 3.4.24.20 peptidyl-Lys metalloendopeptidase
EC 3.4.24.21 astacin
EC 3.4.24.22 stromelysin 2
EC 3.4.24.23 matrilysin
EC 3.4.24.24 gelatinase A
EC 3.4.24.25 vibriolysin
EC 3.4.24.26 pseudolysin
EC 3.4.24.27 thermolysin
EC 3.4.24.28 bacillolysin
EC 3.4.24.29 aureolysin
EC 3.4.24.30 coccolysin
EC 3.4.24.31 mycolysin
EC 3.4.24.32 β-lytic metalloendopeptidase
EC 3.4.24.33 peptidyl-Asp metalloendopeptidase
EC 3.4.24.34 neutrophil collagenase
EC 3.4.24.35 gelatinase B
EC 3.4.24.36 leishmanolysin
EC 3.4.24.37 saccharolysin
EC 3.4.24.38 gametolysin
EC 3.4.24.39 deuterolysin
EC 3.4.24.40 serralysin
EC 3.4.24.41 atrolysin B
EC 3.4.24.42 atrolysin C
EC 3.4.24.43 atroxase
EC 3.4.24.44 atrolysin E
EC 3.4.24.45 atrolysin F
EC 3.4.24.46 adamalysin
EC 3.4.24.47 horrilyn
EC 3.4.24.48 ruberlysin
EC 3.4.24.49 bothropasin
EC 3.4.24.50 bothrolysin
EC 3.4.24.51 ophiolysin
EC 3.4.24.52 trimere lysin I
EC 3.4.24.53 trimere lysin II
EC 3.4.24.54 macrolysin
EC 3.4.24.55 pitrilysin
EC 3.4.24.56 insulysin
EC 3.4.24.57 O-sialoglycoprotein endopeptidase
EC 3.4.24.58 Russellysin
EC 3.4.24.59 mitochondrial intermediate peptidase
EC 3.4.24.60 dactyllysin
EC 3.4.24.61 nardilysin
EC 3.4.24.62 magnolysin
EC 3.4.24.63 meprin B
EC 3.4.24.64 mitochondrial processing peptidase
EC 3.4.24.65 macrophage elastase
EC 3.4.24.66 chorolyisin L
EC 3.4.24.67 chorolyisin H
EC 3.4.24.68 tentoxylisin
EC 3.4.24.69 bontoxilysin
EC 3.4.24.70 oligopeptidase A
EC 3.4.24.71 endothelin-converting enzyme
EC 3.4.24.72 fibrolase
EC 3.4.24.73 jararhagin
EC 3.4.24.74 fragilysin
EC 3.4.24.75 lysostaphin
EC 3.4.24.76 flavastacin
EC 3.4.24.77 snapalysin
EC 3.4.24.78 gpr endopeptidase
EC 3.4.24.79 pappalysin-1
EC 3.4.24.80 membrane-type matrix metalloproteinase-1
EC 3.4.24.81 ADAM10 endopeptidase
EC 3.4.24.82 ADAMTS-4 endopeptidase
EC 3.4.24.83 anthrax lethal factor endopeptidase
EC 3.4.24.84 Ste24 endopeptidase
EC 3.4.24.85 S2P endopeptidase
EC 3.4.24.86 ADAM 17 endopeptidase

EC 3.4.25 Threonine endopeptidases

EC 3.4.25.1 proteasome endopeptidase complex

EC 3.4.99 Endopeptidases of unknown catalytic mechanism

EC 3.4.99.1 now EC 3.4.23.28
EC 3.4.99.2 deleted
EC 3.4.99.3 deleted
EC 3.4.99.4 now EC 3.4.23.12
EC 3.4.99.5 now EC 3.4.24.3
EC 3.4.99.6 now EC 3.4.24.21
EC 3.4.99.7 deleted
EC 3.4.99.8 deleted
EC 3.4.99.9 deleted
EC 3.4.99.10 now EC 3.4.24.56 (supplement 3)
EC 3.4.99.11 deleted
EC 3.4.99.12 deleted
EC 3.4.99.13 now EC 3.4.24.32
EC 3.4.99.14 deleted
EC 3.4.99.15 deleted
EC 3.4.99.16 deleted
EC 3.4.99.17 deleted
EC 3.4.99.18 deleted
EC 3.4.99.19 now EC 3.4.23.15
EC 3.4.99.20 deleted
EC 3.4.99.21 deleted
EC 3.4.99.22 now EC 3.4.24.29
EC 3.4.99.23 deleted
EC 3.4.99.24 deleted
EC 3.4.99.25 deleted, included in EC 3.4.23.21
EC 3.4.99.26 now covered by EC 3.4.24.73, EC 3.4.21.68
EC 3.4.99.27 deleted
EC 3.4.99.28 now EC 3.4.21.60
EC 3.4.99.29 deleted
EC 3.4.99.30 deleted, included in EC 3.4.24.20
EC 3.4.99.31 deleted, included in EC 3.4.24.15
EC 3.4.99.32 now EC 3.4.24.20
EC 3.4.99.33 deleted
EC 3.4.99.34 deleted
EC 3.4.99.35 now EC 3.4.23.36 (supplement 2)
EC 3.4.99.36 now EC 3.4.21.89 (supplement 2)
EC 3.4.99.37 deleted
EC 3.4.99.38 now EC 3.4.23.17
EC 3.4.99.39 deleted
EC 3.4.99.40 deleted
EC 3.4.99.41 now EC 3.4.24.64 (supplement 2)
EC 3.4.99.42 deleted
EC 3.4.99.43 now EC 3.4.23.42 (supplement 6)
EC 3.4.99.44 now EC 3.4.24.55 (supplement 1)
EC 3.4.99.45 now EC 3.4.24.56 (supplement 1)
EC 3.4.99.46 now EC 3.4.25.1 (supplement 6)

EC 3.5 Acting on Carbon-Nitrogen Bonds, other than Peptide Bonds

EC 3.5.1 In Linear Amides

EC 3.5.1.1 asparaginase
EC 3.5.1.2 glutaminase
EC 3.5.1.3 ω-amidase
EC 3.5.1.4 amidase
EC 3.5.1.5 urease
EC 3.5.1.6 β-ureidopropionase
EC 3.5.1.7 ureidosuccinase
EC 3.5.1.8 formylaspartate deformylase
EC 3.5.1.9 arylformamidase
EC 3.5.1.10 formyltetrahydrofolate deformylase
EC 3.5.1.11 penicillin amidase
EC 3.5.1.12 biotimidase
EC 3.5.1.13 aryl-acylamidase
EC 3.5.1.14 aminoacylase
EC 3.5.1.15 aspartoacylase
EC 3.5.1.16 acetylornithine deacetylase
EC 3.5.1.17 acyl-lysine deacetylase
EC 3.5.1.18 succinyl-diaminopimelate desuccinylase
EC 3.5.1.19 nicotinamidase
EC 3.5.1.20 citrullinase
EC 3.5.1.21 N-acetyl-β-alanine deacetylase
EC 3.5.1.22 pantothenase
EC 3.5.1.23 ceramidase
EC 3.5.1.24 choloiglycine hydrolase
EC 3.5.1.25 N-acetylglucosamine-6-phosphate deacetylase
EC 3.5.1.26 N^4-[β-N-acetylglucosaminy1]-L-asparaginase
EC 3.5.1.27 N-formylmethionylaminoacyl-tRNA deformylase
EC 3.5.1.28 N-acetylmuramoyl-L-alanine amidase
EC 3.5.1.29 2-(acetamidomethylene)succinate hydrolase
EC 3.5.1.30 5-aminopentanamide
EC 3.5.1.31 formylmethionine deformylase
EC 3.5.1.32 hippurate hydrolase
EC 3.5.1.33 N-acetylglucosamine deacetylas
EC 3.5.1.34 deleted, same as EC 3.4.13.5
EC 3.5.1.35 D-glutaminase
EC 3.5.1.36 N-methyl-2-oxoglutaramate hydrolase
EC 3.5.1.37 deleted, same as EC 3.5.1.26
EC 3.5.1.38 glutamin-(asparagin)-ase
EC 3.5.1.39 alkylamidase
EC 3.5.1.40 acylagmatine amidase
EC 3.5.1.41 chitin deacetylase
EC 3.5.1.42 nicotinamide-nucleotide amidase
EC 3.5.1.43 peptidyl-glutaminase
EC 3.5.1.44 protein-glutamine glutaminase
EC 3.5.1.45 now EC 6.3.4.6
EC 3.5.1.46 6-aminohexanoate-dimer hydrolase
EC 3.5.1.47 N-acetyldiaminopimelate deacetylase
EC 3.5.1.48 acetyl spermidine deacetylase
EC 3.5.1.49 formamidase
EC 3.5.1.50 pentanamidase
EC 3.5.1.51 4-acetamidobutyryl-CoA deacetylase
EC 3.5.1.52 peptid-\(N^\alpha-(N\text{-acetyl-}\beta\text{-glucosaminy})\)asparagine amidase
EC 3.5.1.53 N-carbamoylputrescine amidase
EC 3.5.1.54 allophanate hydrolase
EC 3.5.1.55 long-chain-fatty-acyl-glutamate deacylase
EC 3.5.1.56 N,N-dimethylformamidase
EC 3.5.1.57 tryptophanamidase
EC 3.5.1.58 N-benzyloxy carbonylglycine hydrolase
EC 3.5.1.59 N-carbamoylsarcosine amidase
EC 3.5.1.60 N-(long-chain-acyl)ethanolamine deacylase
EC 3.5.1.61 mimosinase
EC 3.5.1.62 acetylputrescine deacetylase
EC 3.5.1.63 4-acetamidobutyrate deacetylase
EC 3.5.1.64 N\(^\alpha\)-benzoyloxy carbonylleucine hydrolase
EC 3.5.1.65 theanine hydrolase
EC 3.5.1.66 2-(hydroxymethyl)-3-(acetamidomethylene)succinate hydrolase
EC 3.5.1.67 4-methylene glutaminase
EC 3.5.1.68 N-formyl glutamate deformylase
EC 3.5.1.69 glycosphingolipid deacylase
EC 3.5.1.70 aculeacin-A deacylase
EC 3.5.1.71 N-feruloylglycine deacylase
EC 3.5.1.72 D-benzoylarginine-4-nitroanilide amidase
EC 3.5.1.73 carnitini naminase
EC 3.5.1.74 chenodeoxy cholo yltaurine hydrolase
EC 3.5.1.75 ureathanase
EC 3.5.1.76 arylalkyl acylamidase
EC 3.5.1.77 N-carbamoyl-D-amino acid hydrolase
EC 3.5.1.78 glutathionyl spermidine amidase
EC 3.5.1.79 phthialyl amidase
EC 3.5.1.80 deleted, identical to EC 3.5.1.25
EC 3.5.1.81 N-acetyl-D-amino acid deacylase
EC 3.5.1.82 N-acetyl-D-glutamate deacylase
EC 3.5.1.83 N-acetyl-D-aspartate deacylase
EC 3.5.1.84 biuret amidohydrolase
EC 3.5.1.85 (S)-N-acetyl-1-phenylethylamine hydrolase
EC 3.5.1.86 mandelamide amidase
EC 3.5.1.87 N-carbamoyl-L-amino-acid hydrolase
EC 3.5.1.88 peptide deformylase
EC 3.5.1.89 N-acetylglucosaminylphosphatidylinositol deacetylase
EC 3.5.1.90 adenosylcobinamide hydrolase
EC 3.5.1.91 N-substituted formamide deformylase
EC 3.5.1.92 pantetheine hydrolase
EC 3.5.1.93 glutaryl-7-aminoccephalosporanic-acid acylase
EC 3.5.1.94 γ-glutamyl-γ-amino butyrate hydrolase
EC 3.5.1.95 N-malonylurea hydrolase
EC 3.5.1.96 succinylglutamate desuccinylase

EC 3.5.2 In Cyclic Amides

EC 3.5.2.1 barbiturase
EC 3.5.2.2 dihydropryimidinase
EC 3.5.2.3 dihydroorotase
EC 3.5.2.4 carboxymethylhydantoinase
EC 3.5.2.5 allantoicase
EC 3.5.2.6 β-lactamase
EC 3.5.2.7 imidazolonepropionase
EC 3.5.2.8 deleted, included in EC 3.5.2.6
EC 3.5.2.9 5-oxoprolinase (ATP-hydrolysing)
EC 3.5.2.10 creatinase
EC 3.5.2.11 L-lysine-lactamase
EC 3.5.2.12 6-aminooxoate-cyclic-dimer hydrolase
EC 3.5.2.13 2,5-dioxopiperazine hydrolase
EC 3.5.2.14 N-methylhydantoinase (ATP-hydrolysing)
EC 3.5.2.15 cyanuric acid amidohydrolase
EC 3.5.2.16 maleimide hydrolase
EC 3.5.2.17 hydroxyisoulate hydrolase

EC 3.5.3 In Linear Amidines

EC 3.5.3.1 arginase
EC 3.5.3.2 guanidinoacetase
EC 3.5.3.3 creatinase
EC 3.5.3.4 allantoicase
EC 3.5.3.5 formiminooaspartate deiminase
EC 3.5.3.6 arginine deiminase
EC 3.5.3.7 guanidinobutyrase
EC 3.5.3.8 formimidoylglutamase
EC 3.5.3.9 allantoate deiminase
EC 3.5.3.10 D-arginase
EC 3.5.3.11 agmatinase
EC 3.5.3.12 agmatine deiminase
EC 3.5.3.13 formimino glutamate deiminase
EC 3.5.3.14 amidinospartase
EC 3.5.3.15 protein-arginine deiminase
EC 3.5.3.16 methylguanidinase
EC 3.5.3.17 guanidino propionase
EC 3.5.3.18 dimethylargininase
EC 3.5.3.19 ureidoglycolate hydrolase
EC 3.5.3.20 diguanidinobutanase
EC 3.5.3.21 methylenediurea deaminase
EC 3.5.3.22 proclavaminate amidohydrolase
EC 3.5.3.23 \( N \)-succinylarginine dihydrolase

**EC 3.5.4 In Cyclic Amidines**

- EC 3.5.4.1 cytosine deaminase
- EC 3.5.4.2 adenine deaminase
- EC 3.5.4.3 guanine deaminase
- EC 3.5.4.4 adenosine deaminase
- EC 3.5.4.5 cytidine deaminase
- EC 3.5.4.6 AMP deaminase
- EC 3.5.4.7 ADP deaminase
- EC 3.5.4.8 aminoimidazolase
- EC 3.5.4.9 methylenetetrahydrofolate cyclohydrolase
- EC 3.5.4.10 IMP cyclohydrolase
- EC 3.5.4.11 pterin deaminase
- EC 3.5.4.12 dCMP deaminase
- EC 3.5.4.13 dCTP deaminase
- EC 3.5.4.14 deoxycytidine deaminase
- EC 3.5.4.15 guanosine deaminase
- EC 3.5.4.16 GTP cyclohydrolase I
- EC 3.5.4.17 adenosine-phosphate deaminase
- EC 3.5.4.18 ATP deaminase
- EC 3.5.4.19 phosphoribosyl-AMP cyclohydrolase
- EC 3.5.4.20 pyrithiamine deaminase
- EC 3.5.4.21 creatinine deaminase
- EC 3.5.4.22 1-pyrrolene-4-carboxylate deaminase
- EC 3.5.4.23 blastidicin-S deaminase
- EC 3.5.4.24 sepiapterin deaminase
- EC 3.5.4.25 GTP cyclohydrolase II
- EC 3.5.4.26 diaminohydroxyphosphoribosylaminopyrimidine deaminase
- EC 3.5.4.27 methylenetetrahydroflavanopterin cyclohydrolase
- EC 3.5.4.28 \( S \)-adenosylhomocysteine deaminase
- EC 3.5.4.29 GTP cyclohydrolase Ila
- EC 3.5.4.30 dCTP deaminase (dUMP-forming)

**EC 3.5.5 In Nitriles**

- EC 3.5.5.1 nitrilase
- EC 3.5.5.2 ricinine nitrilase
- EC 3.5.5.3 now EC 4.3.99.1
- EC 3.5.5.4 cyanoalanine nitrilase
- EC 3.5.5.5 arylacetonitrilase
- EC 3.5.5.6 bromoxynil nitrilase
- EC 3.5.5.7 aliphatic nitrilase
- EC 3.5.5.8 thiocyanate hydrolase

**EC 3.5.99 In Other Compounds**

- EC 3.5.99.1 riboflavinase
- EC 3.5.99.2 thiaminase
- EC 3.5.99.3 hydroxydechloratrazine ethylaminohydrolase
- EC 3.5.99.4 \( N \)-isopropylammehide isopropylaminohydrolase
- EC 3.5.99.5 2-aminomuconate deaminase
EC 3.5.99.6 glucosamine-6-phosphate deaminase
EC 3.5.99.7 1-aminocyclopropane-1-carboxylate deaminase

**EC 3.6 Acting on Acid Anhydrides**

**EC 3.6.1 In Phosphorus-Containing Anhydrides**

EC 3.6.1.1 inorganic diphosphatase
EC 3.6.1.2 trimetaphosphatase
EC 3.6.1.3 adenosintriphosphatase
EC 3.6.1.4 deleted, included in EC 3.6.1.3
EC 3.6.1.5 apyrase
EC 3.6.1.6 nucleoside-diphosphatase
EC 3.6.1.7 acylphosphatase
EC 3.6.1.8 ATP diphosphatase
EC 3.6.1.9 nucleotide diphosphatase
EC 3.6.1.10 endopolyphosphatase
EC 3.6.1.11 exopolymyphosphatase
EC 3.6.1.12 dCTP diphosphatase
EC 3.6.1.13 ADP-ribose diphosphatase
EC 3.6.1.14 adenosine-tetraphosphatase
EC 3.6.1.15 nucleoside-triphosphatase
EC 3.6.1.16 CDP-glycerol diphosphatase
EC 3.6.1.17 bis(5'-nucleosyl)-triphosphatase (asymmetrical)
EC 3.6.1.18 FAD diphosphatase
EC 3.6.1.19 nucleoside-triphosphate diphosphatase
EC 3.6.1.20 5'-acylphosphoadenosine hydrolase
EC 3.6.1.21 ADP-sugar diphosphatase
EC 3.6.1.22 NAD' diphosphatase
EC 3.6.1.23 dUTP diphosphatase
EC 3.6.1.24 nucleoside phosphoacetylhydrolase
EC 3.6.1.25 triphosphatase
EC 3.6.1.26 CDP-diacylglycerol diphosphatase
EC 3.6.1.27 undecaprenyl-diphosphatase
EC 3.6.1.28 thiamine-triphosphatase
EC 3.6.1.29 bis(5'-adenosyl)-triphosphatase
EC 3.6.1.30 m'G(5')pppN diphosphatase
EC 3.6.1.31 phosphoribosyl-ATP diphosphatase
EC 3.6.1.32 now EC 3.6.4.1
EC 3.6.1.33 now EC 3.6.4.2
EC 3.6.1.34 now EC 3.6.3.14
EC 3.6.1.35 now EC 3.6.3.6
EC 3.6.1.36 now EC 3.6.3.10
EC 3.6.1.37 now EC 3.6.3.9
EC 3.6.1.38 now EC 3.6.3.8
EC 3.6.1.39 thymidine-triphosphatase
EC 3.6.1.40 guanosine-5'-triphosphate, 3'-diphosphate diphosphatase
EC 3.6.1.41 bis(5'-nucleosyl)-tetraphosphatase (symmetrical)
EC 3.6.1.42 guanosine-diphosphatase
EC 3.6.1.43 dolichyl diphosphatase
EC 3.6.1.44 oligosaccharide-diphosphodolichol diphosphatase
EC 3.6.1.45 UDP-sugar diphosphatase
EC 3.6.1.46 now EC 3.6.5.1
EC 3.6.1.47 now EC 3.6.5.2
EC 3.6.1.48 now EC 3.6.5.3
EC 3.6.1.49 now EC 3.6.5.4
EC 3.6.1.50 now EC 3.6.5.5
EC 3.6.1.51 now EC 3.6.5.6
EC 3.6.1.52 diphosphonositol-polyphosphate diphosphatase

EC 3.6.2 In Sulfonyl-Containing Anhydrides

EC 3.6.2.1 adenylylsulfatase
EC 3.6.2.2 phosphoadenylylsulfatase

EC 3.6.3 Acting on acid anhydrides: catalysing transmembrane movement of substances

EC 3.6.3.1 Mg$^{2+}$-ATPase
EC 3.6.3.2 Mg$^{2+}$-importing ATPase
EC 3.6.3.3 Cd$^{2+}$-exporting ATPase
EC 3.6.3.4 Cu$^{2+}$-exporting ATPase
EC 3.6.3.5 Zn$^{2+}$-exporting ATPase
EC 3.6.3.6 H$^{+}$-exporting ATPase
EC 3.6.3.7 Na$^{+}$-exporting ATPase
EC 3.6.3.8 Ca$^{2+}$-transporting ATPase
EC 3.6.3.9 Na$^{+}$/K$^{+}$-exchanging ATPase
EC 3.6.3.10 H$^{+}$/K$^{+}$-exchanging ATPase
EC 3.6.3.11 Cl$^{-}$-transporting ATPase
EC 3.6.3.12 K$^{+}$-transporting ATPase
EC 3.6.3.13 deleted identical to EC 3.6.3.1
EC 3.6.3.14 H$^{+}$-transporting two-sector ATPase
EC 3.6.3.15 Na$^{+}$-transporting two-sector ATPase
EC 3.6.3.16 arsenite-transporting ATPase
EC 3.6.3.17 monosaccharide-transporting ATPase
EC 3.6.3.18 oligosaccharide-transporting ATPase
EC 3.6.3.19 mallose-transporting ATPase
EC 3.6.3.20 glycerol-3-phosphate-transporting ATPase
EC 3.6.3.21 polar-amino-acid-transporting ATPase
EC 3.6.3.22 nonpolar-amino-acid-transporting ATPase
EC 3.6.3.23 oligopeptide-transporting ATPase
EC 3.6.3.24 nickel-transporting ATPase
EC 3.6.3.25 sulfate-transporting ATPase
EC 3.6.3.26 nitrate-transporting ATPase
EC 3.6.3.27 phosphate-transporting ATPase
EC 3.6.3.28 phosphonate-transporting ATPase
EC 3.6.3.29 molybdate-transporting ATPase
EC 3.6.3.30 Fe$^{3+}$-transporting ATPase
EC 3.6.3.31 polyamine-transporting ATPase
EC 3.6.3.32 quaternary-amine-transporting ATPase
EC 3.6.3.33 vitamin B$_{12}$-transporting ATPase
EC 3.6.3.34 iron-chelate-transporting ATPase
EC 3.6.3.35 manganese-transporting ATPase
EC 3.6.3.36 taurine-transporting ATPase
EC 3.6.3.37 guanine-transporting ATPase
EC 3.6.3.38 capsular-polysaccharide-transporting ATPase
EC 3.6.3.39 lipopolysaccharide-transporting ATPase
EC 3.6.3.40 teichoic-acid-transporting ATPase
EC 3.6.3.41 heme-transporting ATPase
EC 3.6.3.42 β-glucan-transporting ATPase
EC 3.6.3.43 peptide-transporting ATPase
EC 3.6.3.44 xenobiotic-transporting ATPase
EC 3.6.3.45 included with EC 3.6.3.44
EC 3.6.3.46 cadmium-transporting ATPase
EC 3.6.3.47 fatty-acyl-CoA-transporting ATPase
EC 3.6.3.48 α-factor-transporting ATPase
EC 3.6.3.49 channel-conductance-controlling ATPase
EC 3.6.3.50 protein-secreting ATPase
EC 3.6.3.51 mitochondrial protein-transporting ATPase
EC 3.6.3.52 chloroplast protein-transporting ATPase
EC 3.6.3.53 Ag⁺-exporting ATPase

EC 3.6.4 Acting on acid anhydrides; involved in cellular and subcellular movement

EC 3.6.4.1 myosin ATPase
EC 3.6.4.2 dynein ATPase
EC 3.6.4.3 microtubule-severing ATPase
EC 3.6.4.4 plus-end-directed kinesin ATPase
EC 3.6.4.5 minus-end-directed kinesin ATPase
EC 3.6.4.6 vesicle-fusing ATPase
EC 3.6.4.7 peroxisome-assembly ATPase
EC 3.6.4.8 proteasome ATPase
EC 3.6.4.9 chaperonin ATPase
EC 3.6.4.10 non-chaperonin molecular chaperone ATPase
EC 3.6.4.11 nucleoplasmin ATPase

EC 3.6.5 Acting on GTP; involved in cellular and subcellular movement

EC 3.6.5.1 heterotrimeric G-protein GTPase
EC 3.6.5.2 small monomeric GTPase
EC 3.6.5.3 protein-synthesizing GTPase
EC 3.6.5.4 signal-recognition-particle GTPase
EC 3.6.5.5 dynamin GTPase
EC 3.6.5.6 tubulin GTPase

EC 3.7 Acting on Carbon-Carbon Bonds

EC 3.7.1 In Ketonic Substances

EC 3.7.1.1 oxaloacetase
EC 3.7.1.2 fumarylacetocetase
EC 3.7.1.3 kynureninase
EC 3.7.1.4 phloretin hydrolase
EC 3.7.1.5 acylpyruvate hydrolase
EC 3.7.1.6 acetylpyruvate hydrolase
EC 3.7.1.7 β-diketone hydrolase
EC 3.7.1.8 2,6-dioxo-6-phenylhexa-3-enoate hydrolase
EC 3.7.1.9 2-hydroxymuconate-semialdehyde hydrolase
EC 3.7.1.10 cyclohexane-1,3-dione hydrolase

EC 3.8 Acting on Halide Bonds

EC 3.8.1 In C-Halide Compounds
EC 3.8.1.1 alkylhalidase
EC 3.8.1.2 (S)-2-haloacid dehalogenase
EC 3.8.1.3 haloacetate dehalogenase
EC 3.8.1.4 now EC 1.97.1.10
EC 3.8.1.5 haloalkane dehalogenase
EC 3.8.1.6 4-chlorobenzoate dehalogenase
EC 3.8.1.7 4-chloro benzoyl-CoA dehalogenase
EC 3.8.1.8 atrazine chlorohydrolase EC 3.8.1.9 (R)-2-haloacid dehalogenase
EC 3.8.1.10 2-haloacid dehalogenase (configuration-inverting)
EC 3.8.1.11 2-haloacid dehalogenase (configuration-retaining)

EC 3.8.2.1 now EC 3.1.8.2

EC 3.9 Acting on Phosphorus-Nitrogen Bonds
EC 3.9.1.1 phosphoamidase

EC 3.10 Acting on Sulfur-Nitrogen Bonds
EC 3.10.1.1 N-sulfoglycosamine sulfohydrodrolase
EC 3.10.1.2 cyclamate sulfohydrodrolase

EC 3.11 Acting on Carbon-Phosphorus Bonds
EC 3.11.1.1 phosphonoacetalddehyde hydrolase
EC 3.11.1.2 phosphonoacetate hydrolase

EC 3.12 Acting on Sulfur-Sulfur Bonds
EC 3.12.1.1 trithionate hydrolase

EC 3.13 Acting on Carbon-Sulfur Bonds
EC 3.13.1.1 UDP-sulfoquinovose synthase
EC 3.13.1.2 deleted probably EC 4.4.1.21
EC 3.13.1.3 2'-hydroxybiphenyl-2-sulfinate desulfinase

EC 4. Lyases

EC 4.1 Carbon-Carbon Lyases

EC 4.1.1 Carboxy-Lyases
EC 4.1.1.1 pyruvate decarboxylase
EC 4.1.1.2 oxalate decarboxylase
EC 4.1.1.3 oxaloacetate decarboxylase
EC 4.1.1.4 acetoacetate decarboxylase
EC 4.1.1.5 acetylacetate decarboxylase
EC 4.1.1.6 aconitate decarboxylase
EC 4.1.1.7 benzoylformate decarboxylase
EC 4.1.1.8 oxalyl-CoA decarboxylase
EC 4.1.1.9 malonyl-CoA decarboxylase
EC 4.1.1.10 deleted, included in EC 4.1.1.12
EC 4.1.1.11 aspartate 1-decarboxylase
EC 4.1.1.12 aspartate 4-decarboxylase
EC 4.1.1.13 deleted
EC 4.1.1.14 valine decarboxylase
EC 4.1.1.15 glutamate decarboxylase
EC 4.1.1.16 hydroxy glutamate decarboxylase
EC 4.1.1.17 ornithine decarboxylase
EC 4.1.1.18 lysine decarboxylase
EC 4.1.1.19 arginine decarboxylase
EC 4.1.1.20 diaminopimelate decarboxylase
EC 4.1.1.21 phosphoribosylaminomimidazole carboxylase
EC 4.1.1.22 histidine decarboxylase
EC 4.1.1.23 orotidine-5'-phosphate decarboxylase
EC 4.1.1.24 aminobenzoate decarboxylase
EC 4.1.1.25 tyrosine decarboxylase
EC 4.1.1.26 deleted, included in EC 4.1.1.28
EC 4.1.1.27 deleted, included in EC 4.1.1.28
EC 4.1.1.28 aromatic-L-amino-acid decarboxylase
EC 4.1.1.29 sulfoualanine decarboxylase
EC 4.1.1.30 pantothoeyltycisteine decarboxylase
EC 4.1.1.31 phosphoenolpyruvate carboxylase
EC 4.1.1.32 phosphoenolpyruvate carboxykinase (GTP)
EC 4.1.1.33 diphosphoehemalunate decarboxylase
EC 4.1.1.34 dehydro-L-gulonate decarboxylase
EC 4.1.1.35 UDP-glucuronate decarboxylase
EC 4.1.1.36 phosphopantothenoylcysteine decarboxylase
EC 4.1.1.37 uroporphyrinogen decarboxylase
EC 4.1.1.38 phosphoenolpyruvate carboxykinase (diphosphate)
EC 4.1.1.39 ribulose-bisphosphate carboxylase
EC 4.1.1.40 hydroxypyruvate decarboxylase
EC 4.1.1.41 methylmalonyl-CoA decarboxylase
EC 4.1.1.42 carnitine decarboxylase
EC 4.1.1.43 phenylpyruvate decarboxylase
EC 4.1.1.44 4-carboxyymuconolactone decarboxylase
EC 4.1.1.45 aminocarboxymuconate-semialdehyde decarboxylase
EC 4.1.1.46 o-pyrocathechuate decarboxylase
EC 4.1.1.47 tartronate-semialdehyde synthase
EC 4.1.1.48 indole-3-glycerol-phosphate synthase
EC 4.1.1.49 phosphoenolpyruvate carboxykinase (ATP)
EC 4.1.1.50 adenosylmethionine decarboxylase
EC 4.1.1.51 3-hydroxy-2-methylpyridine-4,5-dicarboxylate 4-decarboxylase
EC 4.1.1.52 6-methylsalicylate decarboxylase
EC 4.1.1.53 phenylalanine decarboxylase
EC 4.1.1.54 dihydroyxyfumarate decarboxylase
EC 4.1.1.55 4,5-dihydroxyphthalate decarboxylase
EC 4.1.1.56 3-oxolaurate decarboxylase
EC 4.1.1.57 methionine decarboxylase
EC 4.1.1.58 orsellinate decarboxylase
EC 4.1.1.59 gallate decarboxylase
EC 4.1.1.60 stipitationate decarboxylase
EC 4.1.1.61 4-hydroxybenzoate decarboxylase
EC 4.1.1.62 gentisate decarboxylase
EC 4.1.1.63 protocatechuate decarboxylase
EC 4.1.1.64 2,2-dialkyglycine decarboxylase (pyruvate)
EC 4.1.1.65 phosphatidylserine decarboxylase
EC 4.1.1.66 uracil-5-carboxylate decarboxylase
EC 4.1.1.67 UDP-galacturonate decarboxylase
EC 4.1.1.68 5-oxopent-3-ene-1,2,5-tricarboxylate decarboxylase
EC 4.1.1.69 3,4-dihydroxyphthalate decarboxylase
EC 4.1.1.70 glutaconyl-CoA decarboxylase
EC 4.1.1.71 2-oxoglutarate decarboxylase
EC 4.1.1.72 branched-chain-2-oxoacid decarboxylase
EC 4.1.1.73 tartrate decarboxylase
EC 4.1.1.74 indolepyruvate decarboxylase
EC 4.1.1.75 5-guanidino-2-oxopentanoate decarboxylase
EC 4.1.1.76 aryImalonate decarboxylase
EC 4.1.1.77 4-oxalocrotonate decarboxylase
EC 4.1.1.78 acetylenedicarboxylate decarboxylase
EC 4.1.1.79 sulfopyruvate decarboxylase
EC 4.1.1.80 4-hydroxyphenylpyruvate decarboxylase
EC 4.1.1.81 threonine-phosphatic decarboxylase
EC 4.1.1.82 phosphonopyruvate decarboxylase
EC 4.1.1.83 4-hydroxyphenylacetae decarboxylase
EC 4.1.1.84 D-dopachrome decarboxylase
EC 4.1.1.85 3-dehydro-L-gulonate-6-phosphate decarboxylase
EC 4.1.1.86 diaminobutyrate decarboxylase

EC 4.1.2 Aldehyde-Lyases

EC 4.1.2.1 deleted, included in EC 4.1.3.16
EC 4.1.2.2 ketotetrose-phosphate aldolase
EC 4.1.2.3 deleted
EC 4.1.2.4 deoxyribose-phosphate aldolase
EC 4.1.2.5 threonine aldolase
EC 4.1.2.6 deleted
EC 4.1.2.7 deleted, included in EC 4.1.2.13
EC 4.1.2.8 indole-3-glycerol-phosphate lyase
EC 4.1.2.9 phosphoketolase
EC 4.1.2.10 mandelonitrile lyase
EC 4.1.2.11 hydroxymandelonitrile lyase
EC 4.1.2.12 ketopantoalcoholase
EC 4.1.2.13 fructose-bisphosphate aldolase
EC 4.1.2.14 2-dehydro-3-deoxy-phosphogluconate aldolase
EC 4.1.2.15 now EC 2.5.1.54
EC 4.1.2.16 now EC 2.5.1.55
EC 4.1.2.17 L-fuculose-phosphate aldolase
EC 4.1.2.18 2-dehydro-3-deoxy-L-pentionate aldolase
EC 4.1.2.19 rhamnulose-1-phosphate aldolase
EC 4.1.2.20 2-dehydro-3-deoxyglucarate aldolase
EC 4.1.2.21 2-dehydro-3-deoxy-6-phosphogalactonate aldolase
EC 4.1.2.22 fructose-6-phosphate phosphoketolase
EC 4.1.2.23 3-deoxy-D-manno-octulosonate aldolase
EC 4.1.2.24 dimethylamline-N-oxide aldolase
EC 4.1.2.25 dihydronicotinphered aldolase
EC 4.1.2.26 phenylserine aldolase
EC 4.1.2.27 sphinganine-1-phosphate aldolase
EC 4.1.2.28 2-dehydro-3-deoxy-D-pentionate aldolase
EC 4.1.2.29 5-dehydro-2-deoxyphosphogluconate aldolase
EC 4.1.2.30 17α-hydroxyprogesterone aldolase
EC 4.1.2.31 deleted, included in EC 4.1.3.16
EC 4.1.2.32 trimethylamine-oxide aldolase
EC 4.1.2.33 fucoesterol-epoxide lyase
EC 4.1.2.34 4-(2-carboxyphenyl)-2-oxobut-3-enoate aldolase
EC 4.1.2.35 propioin synthase
EC 4.1.2.36 lactate aldolase
EC 4.1.2.37 acetone-cyanohydrin lyase
EC 4.1.2.38 benzoin aldolase
EC 4.1.2.39 hydroxynitrilase
EC 4.1.2.40 tagatose-bisphosphate aldolase
EC 4.1.2.41 vanillin synthase

EC 4.1.3 Oxo-Acid-Lyases

EC 4.1.3.1 isocitrate lyase
EC 4.1.3.2 now EC 2.3.3.9
EC 4.1.3.3 N-acetyleneuraminic lyase
EC 4.1.3.4 hydroxymethylglutaryl-CoA lyase
EC 4.1.3.5 now EC 2.3.3.10
EC 4.1.3.6 citrate (pro-3S)-lyase
EC 4.1.3.7 now EC 2.3.3.1
EC 4.1.3.8 now EC 2.3.3.8
EC 4.1.3.9 now EC 2.3.3.11
EC 4.1.3.10 now EC 2.3.3.7
EC 4.1.3.11 now EC 2.3.3.12
EC 4.1.3.12 now EC 2.3.3.13
EC 4.1.3.13 oxalomalate lyase
EC 4.1.3.14 3-hydroxyaspartate aldolase
EC 4.1.3.15 now EC 2.2.1.5
EC 4.1.3.16 4-hydroxy-2-oxoglutarate aldolase
EC 4.1.3.17 4-hydroxy-4-methyl-2-oxoglutarate aldolase
EC 4.1.3.18 now EC 2.2.1.6
EC 4.1.3.19 now EC 2.5.1.56
EC 4.1.3.20 now EC 2.5.1.57
EC 4.1.3.21 now EC 2.3.3.14
EC 4.1.3.22 citramalate lyase
EC 4.1.3.23 now EC 2.3.3.2
EC 4.1.3.24 malyl-CoA lyase
EC 4.1.3.25 citramalyl-CoA lyase
EC 4.1.3.26 3-hydroxy-3-isohexenylglutaryl-CoA lyase
EC 4.1.3.27 anthranilate synthase
EC 4.1.3.28 now EC 2.3.3.3
EC 4.1.3.29 now EC 2.3.3.4
EC 4.1.3.30 methylisocitrate lyase
EC 4.1.3.31 now EC 2.3.3.5
EC 4.1.3.32 2,3-dimethylmalate lyase
EC 4.1.3.33 now EC 2.3.3.6
EC 4.1.3.34 citryl-CoA lyase
EC 4.1.3.35 (1-hydroxyethylcyclohexan-1-yl)acetyl-CoA lyase
EC 4.1.3.36 naphthoate synthase
EC 4.1.3.37 now EC 2.2.1.7
EC 4.1.3.38 aminodeoxychorismate lyase
EC 4.1.3.39 4-hydroxy-2-oxovalerate aldolase
EC 4.1.99 Other Carbon-Carbon Lyases

EC 4.1.99.1 tryptophanase
EC 4.1.99.2 tyrosine phenol-lyase
EC 4.1.99.3 deoxyribodipyrimidine photo-lyase
EC 4.1.99.4 now EC 3.5.99.7
EC 4.1.99.5 octadecanal decarbonylase
EC 4.1.99.6 now EC 4.2.3.6
EC 4.1.99.7 now EC 4.2.3.9
EC 4.1.99.8 now EC 4.2.3.14
EC 4.1.99.9 now EC 4.2.3.15
EC 4.1.99.10 now EC 4.2.3.16
EC 4.1.99.11 benzylsuccinate synthase

EC 4.2 Carbon-Oxygen Lyases

EC 4.2.1 Hydro-Lyases

EC 4.2.1.1 carbonate dehydratase
EC 4.2.1.2 fumarate hydratase
EC 4.2.1.3 aconitate hydratase
EC 4.2.1.4 citrate dehydratase
EC 4.2.1.5 arabinonate dehydratase
EC 4.2.1.6 galactonate dehydratase
EC 4.2.1.7 altronate dehydratase
EC 4.2.1.8 mannionate dehydratase
EC 4.2.1.9 dihydroxy-acid dehydratase
EC 4.2.1.10 3-dehydroquinimate dehydratase
EC 4.2.1.11 phosphopyruvate hydratase
EC 4.2.1.12 phosphogluconate dehydratase
EC 4.2.1.13 now EC 4.3.1.17
EC 4.2.1.14 now EC 4.3.1.18
EC 4.2.1.15 now EC 4.4.1.1
EC 4.2.1.16 now EC 4.3.1.19
EC 4.2.1.17 enoyl-CoA hydratase
EC 4.2.1.18 methylglutaconyl-CoA hydratase
EC 4.2.1.19 imidazolglycerol-phosphate dehydratase
EC 4.2.1.20 tryptophan synthase
EC 4.2.1.21 now EC 4.2.1.22
EC 4.2.1.22 cystathionine β-synthase
EC 4.2.1.23 deleted
EC 4.2.1.24 porphobilinogen synthase
EC 4.2.1.25 L-arabinonate dehydratase
EC 4.2.1.26 now EC 4.3.1.21
EC 4.2.1.27 acetylene-carboxylate hydratase
EC 4.2.1.28 propanediol dehydratase
EC 4.2.1.29 now EC 4.99.1.6
EC 4.2.1.30 glycerol dehydratase
EC 4.2.1.31 maleate hydratase
EC 4.2.1.32 L(+)tartrate dehydratase
EC 4.2.1.33 3-isopropylmalate dehydratase
EC 4.2.1.34 (S)-2-methylmalate dehydratase
EC 4.2.1.35 (R)-2-methylmalate dehydratase
EC 4.2.1.36 homoaconitate hydratase  
EC 4.2.1.37 now EC 3.3.2.4  
EC 4.2.1.38 now EC 4.3.1.20  
EC 4.2.1.39 gluconate dehydratase  
EC 4.2.1.40 glucarate dehydratase  
EC 4.2.1.41 5-dehydro-4-deoxyglucarate dehydratase  
EC 4.2.1.42 galactarate dehydratase  
EC 4.2.1.43 2-dehydro-3-deoxy-L-arabinonate dehydratase  
EC 4.2.1.44 myo-inosose-2 dehydratase  
EC 4.2.1.45 CDP-glucose 4,6-dehydratase  
EC 4.2.1.46 dTDP-glucose 4,6-dehydratase  
EC 4.2.1.47 GDP-mannose 4,6-dehydratase  
EC 4.2.1.48 D-glutamate cyclase  
EC 4.2.1.49 urocanate hydratase  
EC 4.2.1.50 pyrazolylalanine synthase  
EC 4.2.1.51 prephenate dehydratase  
EC 4.2.1.52 dihydrodipicolinate synthase  
EC 4.2.1.53 oleate hydratase  
EC 4.2.1.54 lactoyl-CoA dehydratase  
EC 4.2.1.55 3-hydroxybutyryl-CoA dehydratase  
EC 4.2.1.56 itaconyl-CoA hydratase  
EC 4.2.1.57 isoheaxenylglutaconyl-CoA hydratase  
EC 4.2.1.58 crotonoyl-[acyl-carrier-protein] hydratase  
EC 4.2.1.59 3-hydroxyoctanoyl-[acyl-carrier-protein] dehydratase  
EC 4.2.1.60 3-hydroxydecanoyl-[acyl-carrier-protein] dehydratase  
EC 4.2.1.61 3-hydroxypalmitoyl-[acyl-carrier-protein] dehydratase  
EC 4.2.1.62 5α-hydroxysteroid dehydratase  
EC 4.2.1.63 now EC 3.3.2.3  
EC 4.2.1.64 now EC 3.3.2.3  
EC 4.2.1.65 3-cyaanoalanine hydratase  
EC 4.2.1.66 cyanide hydratase  
EC 4.2.1.67 D-fucanate dehydratase  
EC 4.2.1.68 L-fucanate dehydratase  
EC 4.2.1.69 cyanamide hydratase  
EC 4.2.1.70 pseudouridylylate synthase  
EC 4.2.1.71 identical to EC 4.2.1.27  
EC 4.2.1.72 now EC 4.1.1.78  
EC 4.2.1.73 protoaphin-aglucone dehydratase (cyclizing)  
EC 4.2.1.74 long-chain-enoyl-CoA hydratase  
EC 4.2.1.75 uroporphyrinogen-III synthase  
EC 4.2.1.76 UDP-glucose 4,6-dehydratase  
EC 4.2.1.77 trans-L-3-hydroxyproline dehydratase  
EC 4.2.1.78 (S)-norcocaurine synthase  
EC 4.2.1.79 2-methylcitrate dehydratase  
EC 4.2.1.80 2-oxopent-4-enoate hydratase  
EC 4.2.1.81 D(-)-tartrate dehydratase  
EC 4.2.1.82 xylosate dehydratase  
EC 4.2.1.83 4-oxalomesaconate hydratase  
EC 4.2.1.84 nitrile hydratase  
EC 4.2.1.85 dimethylmaleate hydratase  
EC 4.2.1.86 16-dehydroprogesterone hydratase  
EC 4.2.1.86 deleted identical to EC 4.2.1.98  
EC 4.2.1.87 octopamine dehydratase  
EC 4.2.1.88 synephrine dehydratase  
EC 4.2.1.89 carmitine dehydratase
EC 4.2.1.90 L-rhamonate dehydratase
EC 4.2.1.91 arogenate dehydratase
EC 4.2.1.92 hydroperoxide dehydratase
EC 4.2.1.93 ATP-dependent NAD(P)H-hydrate dehydratase
EC 4.2.1.94 scytalone dehydratase
EC 4.2.1.95 kievitone hydratase
EC 4.2.1.96 4a-hydroxytetrahydrobiopterin dehydratase
EC 4.2.1.97 phaseoellidin hydratase
EC 4.2.1.98 16a-hydroxyprogesterone dehydratase
EC 4.2.1.99 2-methylisocitrate dehydratase
EC 4.2.1.100 cyclohexa-1,5-dienecarboxyl-CoA hydratase
EC 4.2.1.101 trans-feruloyl-CoA hydratase
EC 4.2.1.102 now EC 4.2.1.100
EC 4.2.1.103 cyclohexyl-isocyanide hydratase
EC 4.2.1.104 cyanate hydratase
EC 4.2.1.105 2-hydroxyisoflavone dehydratase
EC 4.2.1.106 bile-acid 7α-dehydratase
EC 4.2.1.107 3α,7α,12trihydroxy-5β-cholest-24-enoyl-CoA dehydratase
EC 4.2.1.108 ectoine synthase
EC 4.2.1.109 methylthioribulose 1-phosphate dehydratase

EC 4.2.2 Acting on Polysaccharides

EC 4.2.2.1 hyaluronate lyase
EC 4.2.2.2 pectate lyase
EC 4.2.2.3 poly(β-D-mannuronate) lyase
EC 4.2.2.4 now EC 4.2.2.20 and
EC 4.2.2.5 chondroitin AC lyase
EC 4.2.2.6 oligogalacturonide lyase
EC 4.2.2.7 heparin lyase
EC 4.2.2.8 heparin-sulfate lyase
EC 4.2.2.9 pectate disaccharide-lyase
EC 4.2.2.10 pectin lyase
EC 4.2.2.11 poly(α-L-guluronate) lyase
EC 4.2.2.12 xanthan lyase
EC 4.2.2.13 exo-(1→4)-α-D-glucan lyase
EC 4.2.2.14 glucuronan lyase
EC 4.2.2.15 anhydroisialidase
EC 4.2.2.16 levan fructotransferase (DFA-IV-forming)
EC 4.2.2.17 inulin fructotransferase (DFA-I-forming)
EC 4.2.2.18 inulin fructotransferase (DFA-III-forming)
EC 4.2.2.19 chondroitin B lyase
EC 4.2.2.20 chondroitin-sulfate-ABC endolyase
EC 4.2.2.21 chondroitin-sulfate-ABC exolysase

EC 4.2.3 Acting on phosphates

EC 4.2.3.1 threonine synthase
EC 4.2.3.2 ethanolamine-phosphate phospho-lyase
EC 4.2.3.3 methylglyoxal synthase
EC 4.2.3.4 3-dehydroquininate synthase
EC 4.2.3.5 chorismate synthase
EC 4.2.3.6 trichodiene synthase
EC 4.2.3.7 pentalenene synthase
EC 4.2.3.8 casbene synthase
EC 4.2.3.9 aristolochene synthase
EC 4.2.3.10 (-)-endo-fenchol synthase
EC 4.2.3.11 sabinehydrate synthase
EC 4.2.3.12 6-pyruvoyltetrahydropterin synthase
EC 4.2.3.13 (+)-δ-cadinene synthase
EC 4.2.3.14 pinene synthase
EC 4.2.3.15 myrcene synthase
EC 4.2.3.16 (4S)-limonene synthase
EC 4.2.3.17 taxadiene synthase
EC 4.2.3.18 abietadiene synthase
EC 4.2.3.19 ent-kaurene synthase
EC 4.2.3.20 (R)-limonene synthase
EC 4.2.3.21 vetispiradiene synthase
EC 4.2.3.22 germacradienol synthase
EC 4.2.3.23 germacrene-A synthase
EC 4.2.3.24 amorpha-4,11-diene synthase
EC 4.2.3.25 S-linalool synthase
EC 4.2.3.26 R-linalool synthase

EC 4.2.99 Other Carbon-Oxygen Lyases

EC 4.2.99.1 now EC 4.2.2.2
EC 4.2.99.2 now EC 4.2.3.1
EC 4.2.99.3 now EC 4.2.2.2
EC 4.2.99.4 now EC 4.2.2.3
EC 4.2.99.5 deleted
EC 4.2.99.6 deleted, included in EC 4.2.2.4 and EC 4.2.2.5
EC 4.2.99.7 now EC 4.2.3.2
EC 4.2.99.8 now EC 2.5.1.47
EC 4.2.99.9 now EC 2.5.1.48
EC 4.2.99.10 now EC 2.5.1.49
EC 4.2.99.11 now EC 4.2.3.3
EC 4.2.99.12 carboxymethylxysuccinate lyase
EC 4.2.99.13 now EC 2.5.1.50
EC 4.2.99.14 now EC 2.5.1.51
EC 4.2.99.15 now EC 2.5.1.52
EC 4.2.99.16 now EC 2.5.1.53
EC 4.2.99.17 now EC 4.2.99.14
EC 4.2.99.18 DNA-(apurinic or apyrimidinic site) lyase
EC 4.2.99.19 now EC 4.4.1.23

EC 4.3 Carbon-Nitrogen Lyases

EC 4.3.1 Ammonia-Lyases

EC 4.3.1.1 aspartate ammonia-lyase
EC 4.3.1.2 methylaspartate ammonia-lyase
EC 4.3.1.3 histidine ammonia-lyase
EC 4.3.1.4 formimino tetrahydrofolate cyclodeaminase
EC 4.3.1.5 phenylalanine ammonia-lyase
EC 4.3.1.6 β-alanyl-CoA ammonia-lyase
EC 4.3.1.7 ethanolamine ammonia-lyase
EC 4.3.1.8 now EC 2.5.1.61
EC 4.3.1.9 glucosamine ammonia-lyase
EC 4.3.1.10 serine-sulfate ammonia-lyase
EC 4.3.1.11 dihydroxyphenylalanine ammonia-lyase
EC 4.3.1.12 ornithine cyclodeaminase
EC 4.3.1.13 carbamoyl-serine ammonia-lyase
EC 4.3.1.14 3-aminobutyryl-CoA ammonia-lyase
EC 4.3.1.15 diaminopropionate ammonia-lyase
EC 4.3.1.16 threo-3-hydroxyaspartate ammonia-lyase
EC 4.3.1.17 L-serine ammonia-lyase
EC 4.3.1.18 D-serine ammonia-lyase
EC 4.3.1.19 threonine ammonia-lyase
EC 4.3.1.20 erythro-3-hydroxyaspartate ammonia-lyase
EC 4.3.1.21 identical to EC 4.3.1.9

EC 4.3.2 Amidine-Lyases

EC 4.3.2.1 argininosuccinate lyase
EC 4.3.2.2 adenylosuccinate lyase
EC 4.3.2.3 ureidoglycolate lyase
EC 4.3.2.4 purine imidazole-ring cyclase
EC 4.3.2.5 peptidylamidoglycolate lyase

EC 4.3.3 Amine-Lyases

EC 4.3.3.1 3-ketovaldoxylamine C-N-lyase
EC 4.3.3.2 strictosidine synthase
EC 4.3.3.3 deacetylsopicoside synthase
EC 4.3.3.4 deacetylsopicoside synthase

EC 4.3.99 Other Carbon-Nitrogen Lyases

EC 4.3.99.1 now EC 4.2.1.104

EC 4.4 Carbon-Sulfur Lyases

EC 4.4.1.1 cystathionine γ-lyase
EC 4.4.1.2 homocysteine desulphhydrase
EC 4.4.1.3 dimethylpropiothetin dethiomyethylase
EC 4.4.1.4 alliin lyase
EC 4.4.1.5 lactoylglutathione lyase
EC 4.4.1.6 S-alkylcysteine lyase
EC 4.4.1.7 deleted, included in EC 2.5.1.18
EC 4.4.1.8 cystathionine β-lyase
EC 4.4.1.9 L-3-cyanoalamin synthase
EC 4.4.1.10 cysteine lyase
EC 4.4.1.11 methionine γ-lyase
EC 4.4.1.12 deleted
EC 4.4.1.13 cysteine-S-conjugate β-lyase
EC 4.4.1.14 1-aminocyclopropane-1-carboxylate synthase
EC 4.4.1.15 D-cysteine desulphhydrase
EC 4.4.1.16 selenocysteine lyase
EC 4.4.1.17 holocytochrome-c synthase
EC 4.4.1.18 now EC 1.8.3.5
EC 4.4.1.19 phosphosulfolactate synthase
EC 4.4.1.20 leukotriene-C4 synthase
EC 4.4.1.21 S-ribosylhomocysteine lyase
EC 4.4.1.22 S-(hydroxymethyl)glutathione synthase
EC 4.4.1.23 2-hydroxypropyl-CoM lyase
EC 4.4.1.24 sulfolactate sulfo-lyase
EC 4.4.1.25 L-cysteate sulfo-lyase

EC 4.5 Carbon-Halide Lyases

EC 4.5.1.1 DDT-dehydrochlorinase
EC 4.5.1.2 3-chloro-D-alanine dehydrochlorinase
EC 4.5.1.3 dichloromethane dehalogenase
EC 4.5.1.4 L-2-amino-4-chloropent-4-enoate dehydrochlorinase
EC 4.5.1.5 S-carboxymethylcysteine synthase

EC 4.6 Phosphorus-Oxygen Lyases

EC 4.6.1.1 adenylate cyclase
EC 4.6.1.2 guanylate cyclase
EC 4.6.1.3 now EC 4.2.3.4
EC 4.6.1.4 now EC 4.2.3.5
EC 4.6.1.5 now EC 4.2.3.7
EC 4.6.1.6 cytidylate cyclase
EC 4.6.1.7 now EC 4.2.3.8
EC 4.6.1.8 now EC 4.2.3.10
EC 4.6.1.9 now EC 4.2.3.11
EC 4.6.1.10 now EC 4.2.3.12
EC 4.6.1.11 now EC 4.2.3.13
EC 4.6.1.12 2-C-methyl-D-erythritol 2,4-cyclodiphosphate synthase
EC 4.6.1.13 phosphatidylinositol diacylglycerol-lyase
EC 4.6.1.14 glycosylphosphatidylinositol diacylglycerol-lyase
EC 4.6.1.15 FAD-AMP lyase (cyclizing)

EC 4.99 Other Lyases

EC 4.99.1.1 ferrochelatase
EC 4.99.1.2 alkylmercury lyase
EC 4.99.1.3 sirohydrochlorin cobalochelatase
EC 4.99.1.4 sirohydrochlorin ferrochelatase

EC 4.99.1.5 aliphatic aldoxime dehydratase
EC 4.99.1.6 indoleacetaldoxime dehydratase
EC 4.99.1.7 phenylacetaldoxime dehydratase

EC 5. Isomerases

EC 5.1 Racemases and Epimerases

EC 5.1.1 Acting on Amino Acids and Derivatives

EC 5.1.1.1 alanine racemase
EC 5.1.1.2 methionine racemase
EC 5.1.1.3 glutamate racemase
EC 5.1.1.4 proline racemase
EC 5.1.1.5 lysine racemase
EC 5.1.1.6 threonine racemase
EC 5.1.1.7 diaminopimelate epimerase
EC 5.1.1.8 4-hydroxyproline epimerase
EC 5.1.1.9 arginine racemase
EC 5.1.1.10 amino-acid racemase
EC 5.1.1.11 phenylalanine racemase (ATP-hydrolysing)
EC 5.1.1.12 ornithine racemase
EC 5.1.1.13 aspartate racemase
EC 5.1.1.14 nocardicin-A epimerase
EC 5.1.1.15 2-aminoheptano-6-lactam racemase
EC 5.1.1.16 protein-serine epimerase
EC 5.1.1.17 isopenicillin-N epimerase

EC 5.1.2 Acting on Hydroxy Acids and Derivatives

EC 5.1.2.1 lactate racemase
EC 5.1.2.2 mandelate racemase
EC 5.1.2.3 3-hydroxybutyryl-CoA epimerase
EC 5.1.2.4 acetoin racemase
EC 5.1.2.5 tartrate epimerase
EC 5.1.2.6 isocitrate epimerase

EC 5.1.3 Acting on Carbohydrates and Derivatives

EC 5.1.3.1 ribulose-phosphate 3-epimerase
EC 5.1.3.2 UDP-glucose 4-epimerase
EC 5.1.3.3 aldose 1-epimerase
EC 5.1.3.4 L-ribulose-5-phosphate 4-epimerase
EC 5.1.3.5 UDP-arabinose 4-epimerase
EC 5.1.3.6 UDP-glucuronate 4-epimerase
EC 5.1.3.7 UDP-N-acetylglucosamine 4-epimerase
EC 5.1.3.8 N-acylglucosamine 2-epimerase
EC 5.1.3.9 N-acetylglucosamine-6-phosphate 2-epimerase
EC 5.1.3.10 CDP-paratose 2-epimerase
EC 5.1.3.11 cellobiose epimerase
EC 5.1.3.12 UDP-glucuronate 5'-epimerase
EC 5.1.3.13 dTDP-4-dehydroheptose 3,5-epimerase
EC 5.1.3.14 UDP-N-acetylglucosamine 2-epimerase
EC 5.1.3.15 glucos-6-phosphate 1-epimerase
EC 5.1.3.16 UDP-glucosamine 4-epimerase
EC 5.1.3.17 heparosan-N-sulfate-glucuronate 5-epimerase
EC 5.1.3.18 GDP-mannose 3,5-epimerase
EC 5.1.3.19 chondroitin-glucuronate 5-epimerase
EC 5.1.3.20 ADP-glyceromanno-heptose 6-epimerase
EC 5.1.3.21 maltose epimerase
EC 5.1.3.22 L-ribulose-5-phosphate 3-epimerase

EC 5.1.99 Acting on Other Compounds

EC 5.1.99.1 methylmalonyl-CoA epimerase
EC 5.1.99.2 16-hydroxysteroid epimerase
EC 5.1.99.3 allantoin racemase
EC 5.1.99.4 α-methylacyl-CoA racemase
E.C 5.2 cis-trans-Isomerases

E.C 5.2.1.1 maleate isomerase
E.C 5.2.1.2 maleylacetoacetate isomerase
E.C 5.2.1.3 retinal isomerase
E.C 5.2.1.4 maleylpyruvate isomerase
E.C 5.2.1.5 linoleate isomerase
E.C 5.2.1.6 furylfuramide isomerase
E.C 5.2.1.7 retinol isomerase
E.C 5.2.1.8 peptidylprolyl isomerase
E.C 5.2.1.9 farnesol 2-isomerase
E.C 5.2.1.10 2-chloro-4-carboxymethylenebut-2-en-1,4-olide isomerase
E.C 5.2.1.11 deleted entry

E.C 5.3 Intramolecular Oxidoreductases

E.C 5.3.1 Interconverting Aldoses and Ketoses

E.C 5.3.1.1 triose-phosphate isomerase
E.C 5.3.1.2 deleted
E.C 5.3.1.3 arabinose isomerase
E.C 5.3.1.4 L-arabinose isomerase
E.C 5.3.1.5 xylene isomerase
E.C 5.3.1.6 ribose-5-phosphate isomerase
E.C 5.3.1.7 mannos-6-phosphate isomerase
E.C 5.3.1.8 mannose-6-phosphate isomerase
E.C 5.3.1.9 glucose-6-phosphate isomerase
E.C 5.3.1.10 now EC 3.5.99.6
E.C 5.3.1.11 deleted
E.C 5.3.1.12 glucuronate isomerase
E.C 5.3.1.13 arabinose-5-phosphate isomerase
E.C 5.3.1.14 L-rhamnose isomerase
E.C 5.3.1.15 D-lyxose ketol-isomerase
E.C 5.3.1.16 L-(5-phosphoribosyl)-5-[(5-phosphoribosylamino)methylideneamino]imidazole-4-carboxamide isomerase
E.C 5.3.1.17 4-deoxy-L-threo-5-hexosulose-uronate ketol-isomerase
E.C 5.3.1.18 deleted
E.C 5.3.1.19 now EC 2.6.1.16
E.C 5.3.1.20 ribose isomerase
E.C 5.3.1.21 corticosceroid side-chain-isomerase
E.C 5.3.1.22 hydroxypyruvate isomerase
E.C 5.3.1.23 5-methylthioribose-1-phosphate isomerase
E.C 5.3.1.24 phosphoribosylanthranilate isomerase
E.C 5.3.1.25 L-fucose isomerase
E.C 5.3.1.26 galactose-6-phosphate isomerase

E.C 5.3.2 Interconverting Keto- and Enol-Groups

E.C 5.3.2.1 phenylpyruvate tautomerase
E.C 5.3.2.2 oxaloacetate tautomerase

E.C 5.3.3 Transposing C=C Bonds
EC 5.3.3.1 steroid Δ-isomerase
EC 5.3.3.2 isopentenyl-diphosphate Δ-isomerase
EC 5.3.3.3 vinylacetyl-CoA Δ-isomerase
EC 5.3.3.4 muconolactone Δ-isomerase
EC 5.3.3.5 cholestenol Δ-isomerase
EC 5.3.3.6 methylitaconate Δ-isomerase
EC 5.3.3.7 aconitate Δ-isomerase
EC 5.3.3.8 dodecanoyl-CoA Δ-isomerase
EC 5.3.3.9 prostaglandin-Δ1 Δ-isomerase
EC 5.3.3.10 5-carboxymethyl-2-hydroxymuconate Δ-isomerase
EC 5.3.3.11 isopiperitenone Δ-isomerase
EC 5.3.3.12 L-dopachrome isomerase
EC 5.3.3.13 polyenoic fatty acid isomerase
EC 5.3.3.14 trans-2-decenoyl-[acyl-carrier protein] isomerase

EC 5.3.4 Transposing S-S Bonds
EC 5.3.4.1 protein disulfide-isomerase

EC 5.3.99 Other Intramolecular Oxidoreductases
EC 5.3.99.1 deleted
EC 5.3.99.2 prostaglandin-D synthase
EC 5.3.99.3 prostaglandin-E synthase
EC 5.3.99.4 prostaglandin-I synthase
EC 5.3.99.5 thromboxane-A synthase
EC 5.3.99.6 allene-oxide cyclase
EC 5.3.99.7 styrene-oxide isomerase
EC 5.3.99.8 capsanthin/capsorubin synthase
EC 5.3.99.9 neoxanthin synthase

EC 5.4 Intramolecular Transferases
EC 5.4.1 Transferring Acyl Groups
EC 5.4.1.1 lysolecithin acyltransferase
EC 5.4.1.2 precorrin-8X methyltransferase
EC 5.4.2 PhosphoTransferases (Phosphomutases)
EC 5.4.2.1 phosphoglycerate mutase
EC 5.4.2.2 phosphoglucomutase
EC 5.4.2.3 phosphoacetylglucosamine mutase
EC 5.4.2.4 bisphosphoglycerate mutase
EC 5.4.2.5 phosphoglucomutase (glucose-cofactor)
EC 5.4.2.6 β-phosphoglucomutase
EC 5.4.2.7 phosphopentomutase
EC 5.4.2.8 phosphomannomutase
EC 5.4.2.9 phosphoenolpyruvate mutase
EC 5.4.2.10 phosphogluconosamine mutase

EC 5.4.3 Transferring Amino Groups
EC 5.4.3.1 deleted
EC 5.4.3.2 lysine 2,3-aminomutase
EC 5.4.3.3 β-lysine 5,6-aminomutase
EC 5.4.3.4 D-lysine 5,6-aminomutase
EC 5.4.3.5 D-ornithine 4,5-aminomutase
EC 5.4.3.6 tyrosine 2,3-aminomutase
EC 5.4.3.7 leucine 2,3-aminomutase
EC 5.4.3.8 glutamate-1-semialdehyde 2,1-aminomutase

EC 5.4.4 Transferring Hydroxy Groups

EC 5.4.4.1 (hydroxyamino)benzene mutase
EC 5.4.4.2 isochorismate synthase
EC 5.4.4.3 3-(hydroxyamino)phenol mutase

EC 5.4.99 Transferring Other Groups

EC 5.4.99.1 methylaspartate mutase
EC 5.4.99.2 methylmalonyl-CoA mutase
EC 5.4.99.3 2-acetolactate mutase
EC 5.4.99.4 2-methylene glutarate mutase
EC 5.4.99.5 chorismate mutase
EC 5.4.99.6 now EC 5.4.4.2
EC 5.4.99.7 lanosterol synthase
EC 5.4.99.8 cycloartenol synthase
EC 5.4.99.9 UDP-galactopyranose mutase
EC 5.4.99.10 deleted, included in EC 5.4.99.11
EC 5.4.99.11 isomaltulose synthase
EC 5.4.99.12 tRNA-pseudouridine synthase I
EC 5.4.99.13 isobutyryl-CoA mutase
EC 5.4.99.14 4-carboxymethyl-4-methylbutenolide mutase
EC 5.4.99.15 (1→4)-α-D-glucan 1-α-D-glucosylmutase
EC 5.4.99.16 malto α-D-glucosyltransferase
EC 5.4.99.17 squalene—hopene cyclase
EC 5.4.99.18 5-(carboxyamino)imidazole ribonucleotide mutase

EC 5.5 Intramolecular Lyases

EC 5.5.1.1 muconate cycloisomerase
EC 5.5.1.2 3-carboxy-cis,cis-muconate cycloisomerase
EC 5.5.1.3 tetrahydroxypteridine cycloisomerase
EC 5.5.1.4 inositol-3-phosphate synthase
EC 5.5.1.5 carboxy-cis,cis-muconate cyclase
EC 5.5.1.6 chalcone isomerase
EC 5.5.1.7 chlorouromuconate cycloisomerase
EC 5.5.1.8 bornyl diphasphate synthase
EC 5.5.1.9 cycloecualenal cycloisomerase
EC 5.5.1.10 α-pinen-oxide decyclase
EC 5.5.1.11 dichlorouromuconate cycloisomerase
EC 5.5.1.12 copalyl diphasphate synthase
EC 5.5.1.13 ent-copalyl diphasphate synthase

EC 5.99 Other Isomerases
EC 5.99.1.1 thiocyanate isomerase
EC 5.99.1.2 DNA topoisomerase
EC 5.99.1.3 DNA topoisomerase (ATP-hydrolysing)

EC 6. Ligases

EC 6.1 Forming Carbon-Oxygen Bonds

EC 6.1.1 Ligases Forming Aminoacyl-tRNA and Related Compounds

EC 6.1.1.1 tyrosine—tRNA ligase
EC 6.1.1.2 tryptophan—tRNA ligase
EC 6.1.1.3 threonine—tRNA ligase
EC 6.1.1.4 leucine—tRNA ligase
EC 6.1.1.5 isoleucine—tRNA ligase
EC 6.1.1.6 lysine—tRNA ligase
EC 6.1.1.7 alanine—tRNA ligase
EC 6.1.1.8 deleted
EC 6.1.1.9 valine—tRNA ligase
EC 6.1.1.10 methionine—tRNA ligase
EC 6.1.1.11 serine—tRNA ligase
EC 6.1.1.12 aspartate—tRNA ligase
EC 6.1.1.13 D-alanine—poly(phosphoribitol) ligase
EC 6.1.1.14 glycine—tRNA ligase
EC 6.1.1.15 proline—tRNA ligase
EC 6.1.1.16 cysteine—tRNA ligase
EC 6.1.1.17 glutamate—tRNA ligase
EC 6.1.1.18 glutamine—tRNA ligase
EC 6.1.1.19 arginine—tRNA ligase
EC 6.1.1.20 phenylalanine—tRNA ligase
EC 6.1.1.21 histidine—tRNA ligase
EC 6.1.1.22 asparagine—tRNA ligase
EC 6.1.1.23 aspartate—tRNA ligase
EC 6.1.1.24 glutamate—tRNA ligase
EC 6.1.1.25 lysine—tRNA ligase

EC 6.2 Forming Carbon-Sulfur Bonds

EC 6.2.1 Acid-Thiol Ligases

EC 6.2.1.1 acetate—CoA ligase
EC 6.2.1.2 butyrate—CoA ligase
EC 6.2.1.3 long-chain-fatty-acid—CoA ligase
EC 6.2.1.4 succinate—CoA ligase (GDP-forming)
EC 6.2.1.5 succinate—CoA ligase (ADP-forming)
EC 6.2.1.6 glutarate—CoA ligase
EC 6.2.1.7 cholate—CoA ligase
EC 6.2.1.8 oxalate—CoA ligase
EC 6.2.1.9 malate—CoA ligase
EC 6.2.1.10 acid—CoA ligase (GDP-forming)
EC 6.2.1.11 biotin—CoA ligase
EC 6.2.1.12 4-coumarate—CoA ligase
EC 6.2.1.13 acetate—CoA ligase (ADP-forming)
EC 6.2.1.14 6-carboxyhexanoate—CoA ligase
EC 6.2.1.15 arachidonate—CoA ligase
EC 6.2.1.16 acetoacetate—CoA ligase
EC 6.2.1.17 propionate—CoA ligase
EC 6.2.1.18 citrate—CoA ligase
EC 6.2.1.19 long-chain-fatty-acid—luciferin-component ligase
EC 6.2.1.20 long-chain-fatty-acid—[acyl-carrier-protein] ligase
EC 6.2.1.21 now EC 6.2.1.30
EC 6.2.1.22 [citrate (pro-35)-lyase] ligase
EC 6.2.1.23 dicarboxylate—CoA ligase
EC 6.2.1.24 phytanate—CoA ligase
EC 6.2.1.25 benzoate—CoA ligase
EC 6.2.1.26 O-succinylbenzoate—CoA ligase
EC 6.2.1.27 4-hydroxybenzoate—CoA ligase
EC 6.2.1.28 3α,7α-dihydroxy-5β-cholestanate—CoA ligase
EC 6.2.1.29 deleted now EC 6.2.1.7
EC 6.2.1.30 phenylacetate—CoA ligase
EC 6.2.1.31 2-furoate—CoA ligase
EC 6.2.1.32 anthranilate—CoA ligase
EC 6.2.1.33 4-chlorobenzoate—CoA ligase
EC 6.2.1.34 trans-feruloyl-CoA synthase

EC 6.3 Forming Carbon-Nitrogen Bonds

**EC 6.3.1 Acid-Ammonia (or Amine) Ligases (Amide Synthases)**

EC 6.3.1.1 aspartate—ammonia ligase
EC 6.3.1.2 glutamate—ammonia ligase
EC 6.3.1.3 now EC 6.3.4.13
EC 6.3.1.4 aspartate—ammonia ligase (ADP-forming)
EC 6.3.1.5 NAD⁺ synthase
EC 6.3.1.6 glutamate—ethyleneglutamate ligase
EC 6.3.1.7 4-methyleneglutamate—ammonia ligase
EC 6.3.1.8 glutathionylspermidine synthase
EC 6.3.1.9 trypanothione synthase
EC 6.3.1.10 adenosylcobinamide-phosphate synthase
EC 6.3.1.11 glutamate—putrescine ligase

**EC 6.3.2 Acid—Amino-Acid Ligases (Peptide Synthases)**

EC 6.3.2.1 pantoate—β-alanine ligase
EC 6.3.2.2 glutamate—cysteine ligase
EC 6.3.2.3 glutathione synthase
EC 6.3.2.4 D-alanine—D-alanine ligase
EC 6.3.2.5 phosphopantothenate—cysteine ligase
EC 6.3.2.6 phosphoribosylaminimidazolesuccinocarboxamide synthase
EC 6.3.2.7 UDP-N-acetylmuramoyl-L-alanyl-D-glutamate—L-lysine ligase
EC 6.3.2.8 UDP-N-acetylmuramate—L-alanine ligase
EC 6.3.2.9 UDP-N-acetylmuramoylalanine—D-glutamate ligase
EC 6.3.2.10 UDP-N-acetylmuramoylalanine-tripeptide—D-alanyl-D-alanine ligase
EC 6.3.2.11 carnosine synthase
EC 6.3.2.12 dihydrofolate synthase
EC 6.3.2.13 UDP-N-acetylmuramoylalanin-D-glutamate—2,6-diamino-pimelate ligase
EC 6.3.2.14 2,3-dihydroxybenzoate-serine ligase
EC 6.3.2.15 deleted, due to EC 6.3.2.10
EC 6.3.2.16 D-alanine—alanin-poly(glycerolphosphate) ligase
EC 6.3.2.17 tetrahydrofolate synthase
EC 6.3.2.18 γ-glutamylhistamine synthase
EC 6.3.2.19 ubiquitin—protein ligase
EC 6.3.2.20 indoleacetate—lysine synthetase
EC 6.3.2.21 ubiquitin—calmodulin ligase
EC 6.3.2.22 diphthine—ammonia ligase
EC 6.3.2.23 homoglutathione synthase
EC 6.3.2.24 tyrosine—arginine ligase
EC 6.3.2.25 tubulin—tyrosine ligase
EC 6.3.2.26 N-(5-amino-5-carboxypentanoyl)-L-cysteinyl-D-valine synthase
EC 6.3.2.27 aerobactin synthase
EC 6.3.2.28 L-amino-acid α-ligase

EC 6.3.3 Cyclo-Ligases

EC 6.3.3.1 phosphoribosylformylglycinamidine cyclo-ligase
EC 6.3.3.2 5-formyltetrahydrofolate cyclo-ligase
EC 6.3.3.3 dethiobiotin synthase
EC 6.3.3.4 (carboxyethyl)arginine β-lactam-synthase

EC 6.3.4 Other Carbon-Nitrogen Ligases

EC 6.3.4.1 GMP synthase
EC 6.3.4.2 CTP synthase
EC 6.3.4.3 formate—tetrahydrofolate ligase
EC 6.3.4.4 adenylosuccinate synthase
EC 6.3.4.5 argininosuccinate synthase
EC 6.3.4.6 urea carboxylase
EC 6.3.4.7 ribose-5-phosphate—ammonia ligase
EC 6.3.4.8 imidazolacacetate—phosphoribosylphosphate ligase
EC 6.3.4.9 biotin—[methylmalonyl-CoA-carboxyltransferase] ligase
EC 6.3.4.10 biotin—[propionyl-CoA-carboxylase (ATP-hydrolysing)] ligase
EC 6.3.4.11 biotin—[methylcrotonyl-CoA-carboxylase] ligase
EC 6.3.4.12 glutamate—methylamine ligase
EC 6.3.4.13 phosphoribosylamine—glycine ligase
EC 6.3.4.14 biotin carboxylase
EC 6.3.4.15 biotin—[acetyl-CoA-carboxylase] ligase
EC 6.3.4.16 carbamoyl-phosphate synthase (ammonia)
EC 6.3.4.17 formate—dihydrofolate ligase
EC 6.3.4.18 5-(carboxamino)imidazole ribonucleotide synthase

EC 6.3.5 Carbon-Nitrogen Ligases with Glutamine as Amido-N-Donor

EC 6.3.5.1 NAD⁺ synthase (glutamine-hydrolysing)
EC 6.3.5.2 GMP synthase (glutamine-hydrolysing)
EC 6.3.5.3 phosphoribosylformylglycinamidine synthase
EC 6.3.5.4 asparagine synthase (glutamine-hydrolysing)
EC 6.3.5.5 carbamoyl-phosphate synthase (glutamine-hydrolysing)
EC 6.3.5.6 asparaginyl-tRNA synthase (glutamine-hydrolysing)
EC 6.3.5.7 glutaminyl-tRNA synthase (glutamine-hydrolysing)
EC 6.3.5.8 aminodeoxychorismate synthase
EC 6.3.5.9 hydrogenobyrinic acid a,c-diamide synthase (glutamine-hydrolysing)
EC 6.3.5.10 adenosylcobyric acid synthase (glutamine-hydrolysing)

**EC 6.4 Forming Carbon-Carbon Bonds**

EC 6.4.1.1 pyruvate carboxylase
EC 6.4.1.2 acetyl-CoA carboxylase
EC 6.4.1.3 propionyl-CoA carboxylase
EC 6.4.1.4 methylcrotonoyl-CoA carboxylase
EC 6.4.1.5 geranoyl-CoA carboxylase
EC 6.4.1.6 acetone carboxylase

**EC 6.5 Forming Phosphoric Ester Bonds**

EC 6.5.1.1 DNA ligase (ATP)
EC 6.5.1.2 DNA ligase (NAD⁺)
EC 6.5.1.3 RNA ligase (ATP)
EC 6.5.1.4 RNA-3'-phosphate cyclase

**EC 6.6 Forming Nitrogen—Metal Bonds**

**EC 6.6.1 Forming Coordination Complexes**

EC 6.6.1.1 magnesium chelatase EC 6.6.1.2 cobaltochelatase
Table 2: Isotopes Relevant to the Study of Biology

<table>
<thead>
<tr>
<th>Medical Isotope</th>
<th>Stable, Non-radioactive</th>
<th>Radioactive, Unstable</th>
</tr>
</thead>
</table>
| Hydrogen        | $^1$H (protium) – 99.985%  
                 | $^2$H (deuterium) = $^2$H – 0.015% | $^3$H (tritium) |
| Carbon          | $^{12}$C – 98.89%       |                       | $^{14}$C |
|                 | $^{13}$C – 1.11%       |                       | |
| Oxygen          | $^{16}$O – 99.759%     |                       | $^{15}$O |
|                 | $^{17}$O – 0.037% [MRI scans] |                       | $^{19}$O |
|                 | $^{18}$O – 0.204% [PET scans] |                       | |
| Nitrogen        | $^{14}$N – 99.63%      |                       | No convenient |
|                 | $^{15}$N – 0.37% [biochemical tracers] |                       | |
| Sulfur          | $^{32}$S – 95.00%      |                       | $^{35}$S (other S-based radioisotopes very short lived) |
|                 | $^{33}$S – 0.76%       |                       | |
|                 | $^{34}$S – 4.22%       |                       | |
|                 | $^{36}$S – 0.014%      |                       | |

The table shows examples of stable and non-stable isotopes that may have applications in biology (medicine), including application to human breath analysis and the new intelligent chemical entity (NICE) concept outlined in this application. Using isotopic labels in breath analysis has many advantages including but not limited to 1) creating a distinctive “fingerprint” in the breath, which can be used to distinguish labeled compounds from endogenous compounds already present in the body from natural metabolism or diet (e.g., ingestion of food, flavoring additives, drugs or excipients of drugs) and 2) can produce changes in the detection characteristics (e.g., shifts in the absorption spectra using FTIR) that make these molecules easily distinguishable from major analytical interferants in biological media. The % data indicate the percent of all atoms of that particular element in this isotopic form.
<table>
<thead>
<tr>
<th>No.</th>
<th>Compound Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(2 Or 5 Or 6)-Methoxy-3-Methylpyrazine</td>
</tr>
<tr>
<td>2</td>
<td>(2,6,6-Trimethyl-2-Hydroxycyclohexyldiene)Acetic Acid Gamma-Lactone</td>
</tr>
<tr>
<td>3</td>
<td>(2-Furyl)-2-Propanone</td>
</tr>
<tr>
<td>4</td>
<td>(E)-2-(2-Octenyl)Cyclopentanone</td>
</tr>
<tr>
<td>5</td>
<td>(E)-2-(3,7-Dimethyl-2,6-Octadienyl)Cyclopentanone</td>
</tr>
<tr>
<td>6</td>
<td>(E)-2-Decenoic Acid</td>
</tr>
<tr>
<td>7</td>
<td>(E)-2-Heptenoic Acid</td>
</tr>
<tr>
<td>8</td>
<td>(E)-2-Hexenyl Butyrate</td>
</tr>
<tr>
<td>9</td>
<td>(E)-2-Hexenyl Formate</td>
</tr>
<tr>
<td>10</td>
<td>(E)-2-Hexenyl Isovalerate</td>
</tr>
<tr>
<td>11</td>
<td>(E)-2-Hexenyl Propionate</td>
</tr>
<tr>
<td>12</td>
<td>(E)-2-Hexenyl Valerate</td>
</tr>
<tr>
<td>13</td>
<td>(E)-2-Nonenoic Acid</td>
</tr>
<tr>
<td>14</td>
<td>(E)-2-Octen-1-Ol</td>
</tr>
<tr>
<td>15</td>
<td>(E)-2-Octen-4-Ol</td>
</tr>
<tr>
<td>16</td>
<td>(E)-2-Octenoic Acid</td>
</tr>
<tr>
<td>17</td>
<td>(E)-3-(Z)-6-Nonadien-1-Ol</td>
</tr>
<tr>
<td>18</td>
<td>(E)-3,7-Dimethyl-1,5,7-Octatrien-3-Ol</td>
</tr>
<tr>
<td>19</td>
<td>(E)-7-Methyl-3-Octen-2-One</td>
</tr>
<tr>
<td>20</td>
<td>(E,E)-2,4-Decadien-1-Ol</td>
</tr>
<tr>
<td>21</td>
<td>(E,E)-2,4-Octadien-1-Ol</td>
</tr>
<tr>
<td>22</td>
<td>(E,Z)-2,6-Nonadien-1-Ol Acetate</td>
</tr>
<tr>
<td>23</td>
<td>(E,Z)-3,6-Nonadien-1-Ol Acetate</td>
</tr>
<tr>
<td>24</td>
<td>(Z)(Z)-3,6-Nonadien-1-Ol</td>
</tr>
<tr>
<td>25</td>
<td>(Z)-2-Hexen-1-Ol</td>
</tr>
<tr>
<td>26</td>
<td>(Z)-3-Hexenyl (E)-2-Hexenoate</td>
</tr>
<tr>
<td>27</td>
<td>(Z)-3-Hexenyl Anthranilate</td>
</tr>
<tr>
<td>28</td>
<td>(Z)-3-Hexenyl Isobutyrate</td>
</tr>
<tr>
<td>29</td>
<td>(Z)-3-Hexenyl Propionate</td>
</tr>
<tr>
<td>30</td>
<td>(Z)-3-Hexenyl Pyruvate</td>
</tr>
<tr>
<td>31</td>
<td>(Z)-3-Hexenyl Valerate</td>
</tr>
<tr>
<td>32</td>
<td>(Z)-3-Hexenyl(E)-2-Methyl-2-Butenoate</td>
</tr>
<tr>
<td>33</td>
<td>(Z)-4-Hepten-1-Ol</td>
</tr>
<tr>
<td>34</td>
<td>(Z)-4-Hydroxy-6-Dodecenoic Acid Lactone</td>
</tr>
<tr>
<td>35</td>
<td>(Z)-5-Octenyl Propionate</td>
</tr>
<tr>
<td>36</td>
<td>1-(2-Furyl)-1,3-Butanedione</td>
</tr>
<tr>
<td>37</td>
<td>1-(4-Methoxyphenyl)-4-Methyl-1-Penten-3-One</td>
</tr>
<tr>
<td>38</td>
<td>1-(Methylthio)-2-Butanone</td>
</tr>
<tr>
<td>39</td>
<td>1-(P-Methoxyphenyl)-1-Penten-3-One</td>
</tr>
<tr>
<td>40</td>
<td>1-(P-Methoxyphenyl)-2-Propanone</td>
</tr>
<tr>
<td>41</td>
<td>1,1-Dimethoxyethane</td>
</tr>
<tr>
<td>42</td>
<td>1,2-(Di(1'-Ethoxy)Ethoxy)Propane</td>
</tr>
<tr>
<td>43</td>
<td>1,2,3-Tris((1'-Ethoxy)Ethoxy)-Propane</td>
</tr>
<tr>
<td>44</td>
<td>1,2,5,6-Tetrahydrocuminic Acid</td>
</tr>
<tr>
<td>45</td>
<td>1,2-Butanedithiol</td>
</tr>
<tr>
<td>46</td>
<td>1,2-Dimethoxybenzene</td>
</tr>
<tr>
<td>47</td>
<td>1,2-Ethanedithiol</td>
</tr>
</tbody>
</table>

Table 3: FDA Approved Food Additives
48. 1,2-Propanedithiol
49. 1,3,3-Trimethyl-2-Norbornanyl Acetate
50. 1,3,5-Undecatriene
51. 1,3-Butanediol
52. 1,3-Butylene Glycol
53. 1,3-Diphenyl-2-Propanone
54. 1,3-Nonanediol Acetate (Mixed Esters)
55. 1,3-Propanediol
56. 1,4-Cineole
57. 1,4-Dimethyl-4-Acetyl-1-Cyclohexene
58. 1,4-Dithiane
59. 1,4-Nonanediol Diacetate
60. 1,5,5,9-Tetramethyl-13-Oxatricyclo(8.3.0.0(4,9))Tridecane
61. 1,6-Hexanediol
62. 1,8-Octanediol
63. 1,9-Nonanediol
64. 10-Hydroxymethylene-2-Pinene
65. 10-Undecen-1-YI Acetate
66. 10-Undecenal
67. 10-Undecenoic Acid
68. 12-Methyltridecane
69. 1-Amino-2-Propanol
70. 1-Butanethiol
71. 1-Buten-1-YI Methyl Sulfide
72. 1-Decanol
73. 1-Decen-3-OI
74. 1-Ethoxy-3-Methyl-2-Butene
75. 1-Ethyl-2-Acetylpiperrole
76. 1-Ethylhexyl Tiglate
77. 1-Hexanethiol
78. 1-Hexen-3-OI
79. 1-Hydroxy-2-Butanone
80. 1-Hydroxyethylidene-1,1-Diphosphonic Acid
81. 1-Mercapto-2-Propanone
82. 1-Methyl-1-Cyclopenten-3-One
83. 1-Methyl-2,3-Cyclohexadiene
84. 1-Methyl-2-Acetylpiperoole
85. 1-Methyl-3-Methoxy-4-Isopropylbenzene
86. 1-Methylnapthalene
87. 1-Methylthio-2-Propanone
88. 1-Octanol
89. 1-Octene-3-OI
90. 1-Octen-3-One
91. 1-Octen-3-YI Acetate
92. 1-Octen-3-YI Butyrate
93. 1-Octenyl Succinic Anhydride
94. 1-Penten-3-OI
95. 1-Penten-3-One
96. 1-Phenyl-1,2-Propanedione
97. 1-Phenyl-1-Propanol
98. 1-Phenyl-3 Or 5-Propylypyrazole
99. 1-Phenyl-3-Methyl-3-Pentanol
100. 1-P-Menthene-9-Yl Acetate
101. 1-P-Menthene-8-Thiol
102. 1-Pyrrolidine
103. 2-((Methylthio)Methyl)-2-Butenal
104. 2-(1-Methylpropyl)Thiazole
105. 2-(2-Butyl)-4,5-Dimethyl-3-Thiazoline
106. 2-(2-Methylpropyl)Pyridine
107. 2-(3-Phenylpropyl)Pyridine
108. 2-(3-Phenylpropyl)Tetrahydrofuran
109. 2(4)-Isobutyl-4(2),6-Dimethylthiohydron-4H-1,3,5-Dithiazine
110. 2(4)-Isopropyl-4(2),6-Dimethylthiohydron-4H-1,3,5-Dithiazine
111. 2-(4-Methyl-2-HydroxyphenyI)Propionic Acid-Gamma-Lactone
112. 2-(Methylthio)Ethanol
113. 2-(Methylthiomethyl)-3-Phenylpropenal
114. 2-(P-Tolyl)-Propionaldehyde
115. 2,2'-Dithiodimethylenes-Difuran
116. 2,2'-Dithiodimethylenes-Difuran
117. 2,2,3-Trimethylcyclopent-3-En-1-Yl Acetaldehyde
118. 2,2,4-Trimethyl-1,3-Oxacyclohexane
119. 2,2,6-Trimethyl-6-Vinyltetrahydrofuran
120. 2,2,6-Trimethylcyclohexanone
121. 2,2-Dibromo-3-Nitropropionamide
122. 2,2-Dimethyl-5-(1-Methylpropen-1-Yl) Tetrahydrofuran
123. 2,3 Or 10-Mercaptopyrrole
124. 2,3,4-Trimethyl-3-Pentanol
125. 2,3,5,6-Tetramethylpyrazine
126. 2,3,5-Trimethylpyrazine
127. 2,3,6-Trimethylphenol
128. 2,3-Butanedithiol
129. 2,3-Diethyl-5-Methylpyrazine
130. 2,3-Diethylpyrazine
131. 2,3-Dimethylbenzofuran
132. 2,3-Dimethylpyrazine
133. 2,3-Heptanedione
134. 2,3-Hexanedione
135. 2,3-Pentanedione
136. 2,3-Undecadiene
137. 2,4,5-Trihydroxybutyrophenone
138. 2,4,5-Trimethyl-Delta-3-Oxazoline
139. 2,4,5-Trimethylthiazole
140. 2,4-Dihydroxybenzoic Acid
141. 2,4-Dimethyl-2-Pentenoic Acid
142. 2,4-Dimethyl-5-Acetythiazole
143. 2,4-Dimethyl-5-Vinylthiazole
144. 2,4-Dimethylacetophenone
145. 2,4-Dimethylanisole
146. 2,4-Dimethylbenzaldehyde
147. 2,4-Heptadienial
148. 2,4-Hexadien-1-Ol
149. 2,4-Nonadien-1-Ol
150. 2,4-Nonadienal
151. 2,4-Pentadienal
152. 2,4-Undecadienal
153. 2,5-Diethyl-3-Methylpyrazine
154. 2,5-Diethyltetrahydrofuran
155. 2,5-Dihydroxy-1,4-Dithiane
156. 2,5-Dimethyl-2,5-Dihydroxy-1,4-Dithiane
157. 2,5-Dimethyl-3-Furanthiol
158. 2,5-Dimethyl-3-Mercaptotetrahydrofuran
159. 2,5-Dimethyl-3-Thioisovaleryl furan
160. 2,5-Dimethyl-4-Methoxy-3(2H)-Furanone
161. 2,5-Dimethylpyrazine
162. 2,5-Dimethylpyrrole
163. 2,5-Undecadienal
164. 2,5-Xylenol
165. 2,6,10-Trimethyl-2,6,10-Pentadecatrien-14-One
166. 2,6,6-Trimethyl-1 And 2-Cyclohexen-1-Carboxaldehyde
167. 2,6,6-Trimethyl-1-Cyclohexen-1-Acetaldehyde
168. 2,6,6-Trimethylcyclohexa-2-Ene-1,4-Dione
169. 2,6,6-Trimethylcyclohexa-1,3-Dienyl Methanal
170. 2,6-Dimethoxyphenol
171. 2,6-Dimethyl-10-Methylene-2,6,11-Dodecatrional
172. 2,6-Dimethyl-3-((2-Methyl-3-Furyl)Thio)-4-Heptanone
173. 2,6-Dimethyl-4-Heptanol
174. 2,6-Dimethyl-5-Heptenal
175. 2,6-Dimethyl-6-Hepten-1-OI
176. 2,6-Dimethyloctanal
177. 2,6-Dimethylpyrazine
178. 2,6-Dimethylpyridine
179. 2,6-Dimethylthiophenol
180. 2,6-Nonadien-1-Ol
181. 2,6-Nonadienal Diethyl Acetal
182. 2,6-Xylenol
183. 2,8-Dithianon-4-En-4-Carboxaldehyde
184. 2-Acetyl-2-Thiazoline
185. 2-Acetyl-3,(5 Or 6)-Dimethylpyrazine, Mixture Of
186. 2-Acetyl-3-Ethylpyrazine
187. 2-Acetyl-3-Methylpyrazine
188. 2-Acetyl-5-Methylfuran
189. 2-Acetylpyridine
190. 2-Acetylthiazole
191. 2'-Aminoacetophenone
192. 2-Amyl-5 Or 6-Keto-1,4-Dioxane
193. 2-Benzofurancarboxaldehyde
194. 2-Butanol
195. 2-Butanone
196. 2-Butyl-2-Butenal
197. 2-Butyl-5 Or 6-Keto-1,4-Dioxane
198. 2-Decenal
199. 2-Dodecenal
200. 2-Ethoxythiazole
201. 2-Ethyl-(3 Or 5 Or 6)-Mop(85%) And 2-Methyl-(3 Or 5 Or 6)-op(13%)
202. 2-Ethyl-1,3,3-Trimethyl-2-Norbornanol
203. 2-Ethyl-1-Hexanol
204. 2-Ethyl-2-Heptenal
205. 2-Ethyl-3,(5 Or 6)-Dimethylpyrazine
206. 2-Ethyl-4,5-Dimethylloxazole
207. 2-Ethyl-4-Hydroxy-5-Methyl-3(2H)-Furanone
208. 2-Ethyl-4-Methylthiazole
209. 2-Ethyl-5-Methylpyrazine
210. 2-Ethyl-6-Methylpyrazine
211. 2-Ethylbutyl Acetate
212. 2-Ethylbutyraldehyde
213. 2-Ethylbutyric Acid
214. 2-Ethylfuran
215. 2-Ethylhexanethiol
216. 2-Ethylpyrazine
217. 2-Ethylthiophenol
218. 2-Formyl-6,6-Dimethylbicyclo(3.1.1)Hept-2-Ene
219. 2-Furanmethanethiol Formate
220. 2-Furfurylidenebutyraldehyde
221. 2-Furyl Methyl Ketone
222. 2-Heptanol
223. 2-Heptanone
224. 2-Hepten-4-One
225. 2-Heptenal
226. 2-Heptyl Butyrate
227. 2-Heptylfuran
228. 2-Hexen-1-OL
229. 2-Hexenal
230. 2-Hexenyl Hexanoate, Trans-
231. 2-Hexyl-4-Acetoxytetrahydrofuran
232. 2-Hexyl-5 Or 6-Keto-1,4-Dioxane
233. 2-Hexylidene Cyclopentanone
234. 2-Hydroxy-2-Cyclohexen-1-One
235. 2-Hydroxy-3,5,5-Trimethyl-2-Cyclohexenone
236. 2-Hydroxy-4-Methylbenzaldehyde
237. 2-Hydroxy-5-Methyl-3-Hexanone
238. 2-Hydroxyacetophenone
239. 2-Hydroxymethyl-6,6-Dimethylbicyclo(3.1.1)Hept-2-Enyl Formate
240. 2-Isobutyl-3-Methoxypyrazine
241. 2-Isobutyl-3-Methylpyrazine
242. 2-Isobutythiazole
243. 2-Isopropyl-4-Methylthiazole
244. 2-Isopropyl-5-Methyl-2-Hexenal
245. 2-Isopropyl-N,2,3-Trimethylbutyramide
246. 2-Isoproplyphenol
247. 2-Isopropylpyrazine
248. 2-Keto-4-Butanethiol
249. 2-Mercapto-2-Methyl-1-Pentanol
250. 2-Mercapto-3-Butanol
251. 2-Mercaptomethylpyrazine
252. 2-Mercaptopropionic Acid
253. 2-Methoxy-(3 Or 5 Or 6)-Isopropylpyrazine
254. 2-Methoxy-3-(1-Methylpropyl)Pyrazine
255. 2-Methoxy-4-Methylphenol
256. 2-Methoxy-4-Propylphenol
257. 2-Methoxy-4-Vinylphenol
258. 2-Methoxybenzoic Acid
259. 2-Methyl-(3 Or 5 Or 6)-(Methylthio)Pyrazine (Mixture
260. 2-Methyl-(3 Or 5 Or 6)-Ethoxypyrazine
261. 2-Methyl-1,3-Cyclohexadiene
262. 2-Methyl-1,3-Dithiolane
263. 2-Methyl-1-Butanethiol
264. 2-Methyl-1-Butanol
265. 2-Methyl-1-Propanethiol
266. 2-Methyl-2-(Methylthio)Propanal
267. 2-Methyl-2-Butenal
268. 2-Methyl-2-Octenal
269. 2-Methyl-2-Pentenal
270. 2-Methyl-2-Pentenoic Acid
271. 2-Methyl-3 Or 5 Or 6-(Furfurylthio)Pyrazine (Mixture
272. 2-Methyl-3-(2-Furyl)Acrolein
273. 2-Methyl-3-(Methylthio)Furan
274. 2-Methyl-3-(P-Isopropylphenyl) Propionaldehyde
275. 2-Methyl-3-Buten-2-OI
276. 2-Methyl-3-Furanthiol
277. 2-Methyl-3-Heptanone
278. 2-Methyl-3-Pentenoic Acid
279. 2-Methyl-3-Tetrahydrofuranthiol
280. 2-Methyl-3-Thioacetoxy-4,5-Dihydrofuran
281. 2-Methyl-3-Tolylpropionaldehyde (Mixed O-, M-, P-)
282. 2-Methyl-4-Pentenoic Acid
283. 2-Methyl-4-Phenyl-2-Butanol
284. 2-Methyl-4-Phenyl-2-Butyl Acetate
285. 2-Methyl-4-Phenyl-2-Butyl Isobutyrate
286. 2-Methyl-4-Phenylbutyraldehyde
287. 2-Methyl-4-Propyl-1,3-Oxathiane
288. 2-Methyl-5-(Methylthio)Furan
289. 2-Methyl-5-Isopropylpyrazine
290. 2-Methyl-5-Methoxythiazole
291. 2-Methyl-5-Vinylpyrazine
292. 2-Methylallyl Butyrate
293. 2-Methylbutyl 2-Methylbutyrate
294. 2-Methylbutyl Acetate
295. 2-Methylbutyl Isovalerate
296. 2-Methylbutyr aldehyde
297. 2-Methylbutyric Acid
298. 2-Methylcyclohexanone
299. 2-Methylheptanoic Acid
300. 2-Methylhexanoic Acid
301. 2-Methyloctanal
302. 2-Methylpentanal
303. 2-Methylpropyl-3-Methylbutyrate
304. 2-Methylpyrazine
305. 2-Methyltetrahydrofuran-3-One
306. 2-Methyltetrahydrothiophen-3-One
307. 2-Methylthioacetaldehyde
308. 2-Methylundecanal
309. 2-Methylvaleric Acid
310. 2-Naphthalenthiol
311. 2-Nonanol
312. 2-Nonanone
313. 2-Nonenal
314. 2-Octanol
315. 2-Octanone
316. 2-Octen-4-One
317. 2-Octenal
318. 2-Oxo-3-Phenylpropionic Acid
319. 2-Oxopentanoic Acid
320. 2-Pentadecanone
321. 2-Pentanethiol
322. 2-Pentanol
323. 2-Pentanone
324. 2-Penten-1-Ol
325. 2-Pentenal
326. 2-Pentyl Acetate
327. 2-Pentyl Butyrate
328. 2-Pentyl-1-Buten-3-One
329. 2-Pentyl-3-Methyl-2-Cyclopenten-1-One
330. 2-Pentylfuran
331. 2-Pentylpyridine
332. 2-Phenoxyethyl Isobutyrate
333. 2-Phenyl-2-Butenal
334. 2-Phenyl-3-(2-Furyl)-Prop-2-Enal
335. 2-Phenyl-3-Carbethoxy Furan
336. 2-Phenyl-4-Pentenal
337. 2-Phenylpropiionaldehyde
338. 2-Phenylpropiionaldehyde Dimethyl Acetal
339. 2-Phenylpropyl Butyrate
340. 2-Phenylpropyl Isobutyrate
341. 2-Propanethiol
342. 2-Propionylpyrrole
343. 2-Propionylthiazole
344. 2-Propylpyrazine
345. 2-Pyridinemethanethiol
346. 2-Sec-Butylcyclohexanone
347. 2-Tert-Pentylcyclohexyl Acetate
348. 2-Thienyl Disulfide
349. 2-Thienyl Mercaptan
350. 2-Trans,4-Cis,7-Cis-Tridecatrienial
351. 2-Trans,4-Trans-Decadienal
352. 2-Trans,3,7-Dimethylocta-2,6-Dienyl 2-Ethylbutanoate
353. 2-Trans-6-Cis-Dodecadienal
354. 2-Trans-6-Cis-Nonadienal
355. 2-Trans-6-Trans-Nonadienal
356. 2-Trans-6-Trans-Octadienal
357. 2-Tridecanone
358. 2-Tridecenal
359. 2-Undecanol
360. 2-Undecanone
361. 2-Undecen-1-Ol
362. 2-Undecenal
363. 3-((2-Methyl-3-Furyl)Thio)-4-Heptanone
364. 3(2-Furoylthio)-2,5-Dimethylfuran
365. 3-(2-Furyl)Acrolein
366. 3-(2-Methylpropyl)Pyridine
367. 3-(5-Methyl-2-Furyl)-Butanal
368. 3-(Acetylimino)-2-Methylfuran
369. 3-(Hydroxymethyl)-2-Heptanone
370. 3-(Hydroxymethyl)-2-Octanone
371. 3-(L-Menthoxy)-2-Methylpropane-1,2-Diol
372. 3-(Methylthio)-1-Hexanol
373. 3-(Methylthio)Butanal
374. 3-(Methylthio)Hexyl Acetate
375. 3-(Methylthio)Propanol
376. 3-(Methylthio)Propionaldehyde
377. 3-(Methylthio)Propyl Acetate
378. 3-(P-Isopropylphenyl)Propionaldehyde
379. 3,3,5-Trimethylcyclohexanol
380. 3,4-Dimethoxy-1-Vinylbenzene
381. 3,4-Dimethyl-1,2-Cyclopentadione
382. 3,4-Hexanedione
383. 3,4-Xylenol
384. 3,5,5-Trimethyl-1-Hexanol
385. 3,5,5-Trimethylhexanional
386. 3,5-Diethyl-2-Methylpyrazine
387. 3,5-Dimethyl-1,2,4-Trithioliene
388. 3,5-Dimethyl-1,2-Cyclopentadione
389. 3,5-Octadien-2-One, Trans, Trans-
390. 3,6-Dihydro-4-Methyl-2(2-Methylpropen-1-Yl)-2H-Pyran
391. 3,7-Dimethyl-1-Octanol
392. 3,7-Dimethyl-6-Octenoic Acid
393. 3-Acetyl-2,5-Dimethylfuran
394. 3-Acetyl-2,5-Dimethylthiophene
395. 3-Acetylimercaptohexyl Acetate
396. 3-Acetylpyridine
397. 3-Benzyl-4-Heptanone
398. 3-Butylidenephthalide
399. 3-Carene
400. 3-Decanol
401. 3-Decanone
402. 3-Decen-2-One
403. 3-Ethyl-2,6-Dimethylpyrazine
404. 3-Ethyl-2-Hydroxy-2-Cyclopenten-1-One
405. 3-Ethyl-2-Hydroxy-4-Methylcyclopent-2-En-1-One
406. 3-Ethyl-2-Methylpyrazine
407. 3-Ethylpyridine
408. 3-Heptanol
409. 3-Heptanone
410. 3-Hepten-2-One
411. 3-Heptyl Acetate
412. 3-Heptylhydro-5-Methyl-2(3H)-Furanone
413. 3-Hexanol
414. 3-Hexanone
415. 3-Hexenal
416. 3-Hexenoic Acid
417. 3-Hexenyl 2-Methylbutyrate
418. 3-Hexenyl Crotonate, Cis-
419. 3-Hexenyl Isovalerate
420. 3-Hexenyl Phenylacetate
421. 3-Hydroxy-2-Oxopropionic Acid
422. 3-Hydroxy-2-Pentanone
423. 3-Hydroxy-5-Methyl-2-Hexanone
424. 3-L-Menthoxypropane-1,2-Diol
425. 3-Mercapto-2-Butanone
426. 3-Mercapto-2-Methyl-1-Butanol
427. 3-Mercapto-2-Methyl-1-Pentanol
428. 3-Mercapto-2-Methylpentanal
429. 3-Mercapto-2-Pentanone
430. 3-Mercapto-3-Methyl-1-Butanol
431. 3-Mercapto-3-Methylbutyl Formate
432. 3-Mercaptohexanol
433. 3-Mercaptohexyl Acetate
434. 3-Mercaptohexyl Butyrate
435. 3-Mercaptohexyl Hexanoate
436. 3-Methoxybenzoic Acid
437. 3-Methyl-1,2,4-Trithiane
438. 3-Methyl-1-Cyclopentadecanone
439. 3-Methyl-1-Pentanol
440. 3-Methyl-2-Butanethiol
441. 3-Methyl-2-Butanol
442. 3-Methyl-2-Buten-1-Ol
443. 3-Methyl-2-Butenal
444. 3-Methyl-2-Cyclohexen-1-One
445. 3-Methyl-2-Oxobutanoic Acid
446. 3-Methyl-2-Oxopentanoic Acid
447. 3-Methyl-2-Phenylbutyaldehyde
448. 3-Methyl-3-Buten-2-One
449. 3-Methyl-3-Butenyl Acetate
450. 3-Methyl-3-Phenyl Glycidic Acid Ethyl Ester
451. 3-Methyl-4-Phenyl-3-Butene-2-One
452. 3-Methyl-5-Propyl-2-Cyclohexen-1-One
453. Methylbutanethiol
454. 3-Methylbutyraldehyde
455. 3-Methylcrotonic Acid
456. 3-Methylcyclohexanone
457. 3-Methyl-Gamma-Decalactone
458. 3-Methylpentanoic Acid
459. 3-Methylthiohexenal
460. 3-Methylthiopropyl Isothiocyanate
461. 3-N-Butylphthalide
462. 3-Nonanon-1-OI
463. 3-Nonanon-1-YI Acetate
464. 3-Nonanone
465. 3-Nonen-2-One
466. 3-Nonyl Acetate
467. 3-Octanol
468. 3-Octanone
469. 3-Octen-2-One
470. 3-Octyl Acetate
471. 3-Octyl Formate
472. 3-Oxobutanal, Dimethyl Acetal
473. 3-Oxodecaneoic Acid Glyceride
474. 3-Oxodecapaneoic Acid Glyceride
475. 3-Oxohexadecaneoic Acid Glyceride
476. 3-Oxohexanoic Acid Diglyceride
477. 3-Oxoctanoic Acid Glyceride
478. 3-Oxotetradecaneoic Acid Glyceride
479. 3-Penten-2-One
480. 3-Phenyl-1-Propanol
481. 3-Phenyl-4-Pentenal
482. 3-Phenylpropionaldehyde
483. 3-Phenylpropionic Acid
484. 3-Phenylpropyl Acetate
485. 3-Phenylpropyl Cinnamate
486. 3-Phenylpropyl Formate
487. 3-Phenylpropyl Hexanoate
488. 3-Phenylpropyl Isobutyrate
489. 3-Phenylpropyl Isovalerate
490. 3-Phenylpropyl Propionate
491. 3-Propylidenephthalide
492. 4-((2-Methyl-3-Furyl)Thio)-5-Nonanone
493. 4-((Furanmethyl)Thio)-2-Pentanone
494. 4-(2,6,6-Trimethylcyclohex-1-Enyl)But-2-En-4-One
495. 4-(2,6,6-Trimethylcyclohexa-1,3-Dienyl)But-2-En-4-One
496. 4-(2-Furyl)-3-Buten-2-One
497. 4-(3,4-Methylenedioxyphenyl)-2-Butanone
498. 4-(Methylthio)-2-Butanone
499. 4-(Methylthio)-2-Oxobutanoic Acid
500. 4-(Methylthio)-4-Methyl-2-Pentanone
501. 4-(Methylthio)Butanal
502. 4-(Methylthio)Butanol
503. 4-(P-Acetoxyphenyl)-2-Butanone
504. 4-(P-Hydroxyphenyl)-2-Butanone
505. 4-(P-Methoxyphenyl)-2-Butanone
506. 4-(P-Tolyl)-2-Butanone
507. 4,4-Dibutyl-Gamma-Butyrolactone
508. 4,5,6,7-Tetrahydro-3,6-Dimethylbenzofuran
509. 4,5-Dihydro-2,5-Dimethyl-4-Oxo-3-Furanyl Butyrate
510. 4,5-Dihydro-3(2H)Thiophenone
511. 4,5-Dimethyl-2-Ethyl-3-Thiazoline
512. 4,5-Dimethyl-2-Isobutyl-3-Thiazoline
513. 4,5-Dimethyl-3-Hydroxy-2,5-Dihydrofuran-2-One
514. 4,5-Dimethylthiazole
515. 4,8-Dimethyl-3,7-Nonadien-2-One
516. 4,8-Dimethyl-3,7-Nonadien-2-One, Cis-
517. 4,8-Dimethyl-3,7-Nonadien-2-One, Trans-
518. 4-Acetoxy-2,5-Dimethyl-3(2H)-Furanone
519. 4-Acetyl-2-Methylpyrimidine
520. 4-Acetyl-6-Tert-Butyl-1,1-Dimethylindane
521. 4-Allyl-2,6-Dimethoxyphenol
522. 4-Carvomenthenol
523. 4-Decenal
524. 4-Decenoic Acid
525. 4-Decenyl Acetate, Cis-
526. 4-Ethyl-2,6-Dimethoxyphenol
527. 4-Ethylbenzaldehyde
528. 4-Ethylguaiaicol
529. 4-Ethyloctanoic Acid
530. 4-Heptanone
531. 4-Heptenal Diethyl Acetal
532. 4-Hexen-1-Ol
533. 4-Hexene-3-One
534. 4-Hydroxy-2,5-Dimethyl-3(2H)-Furanone
535. 4-Hydroxy-3-Methyloctanoic Acid Lactone
536. 4-Hydroxy-3-Pentenoic Acid Lactone
537. 4-Hydroxy-4-Methyl-7-Cis-Decanoic Acid Gamma lactone
538. 4-Hydroxy-5-Methyl-3(2H)-Furanone
539. 4-Hydroxybenzaldehyde
540. 4-Hydroxybenzoic Acid
541. 4-Hydroxybenzyl Alcohol
542. 4-Hydroxybutanoic Acid Lactone
543. 4-Hydroxymethyl-2,6-Di-Tertbutylphenol
544. 4-Mercapto-4-Methyl-2-Pentanone
545. 4-Methoxy-2-Methyl-2-Butanethiol
546. 4-Methoxybenzoic Acid
547. 4-Methyl-1-Phenyl-2-Pentanone
548. 4-Methyl-2,3-Pentanedione
549. 4-Methyl-2,6-Dimethoxyphenol
550. 4-Methyl-2-Oxopentanoic Acid
551. 4-Methyl-2-Pentenal
552. 4-Methyl-2-Pentyl-1,3-Dioxolan
553. 4-Methyl-2-Phenyl-2-Pentenal
554. 4-Methyl-3-Penten-2-One
555. 4-Methyl-4-Penten-2-One
556. 4-Methyl-5-Thiazoleethanol
557. 4-Methyl-5-Thiazoleethanol Acetate
558. 4-Methyl-5-Vinythiazole
559. 4'-Methylacetophenone
560. 4-Methylbiphenyl
561. 4-Methylcyclohexanone
562. 4-Methylnonanoic Acid
563. 4-Methyloctanoic Acid
564. 4-Methylpentanoic Acid
565. 4-Methylthiazole
566. 4-Pentenoic Acid
567. 4-Pentenyl Acetate
568. 4-Phenyl-2-Butanol
569. 4-Phenyl-2-Butyl Acetate
570. 4-Phenyl-3-Buten-2-Ol
571. 4-Phenyl-3-Buten-2-One
572. 4-Propenyl-2,6-Dimethoxyphenol
573. 4-Propyl-2,6-Dimethoxyphenol
574. 4-Thujanol
575. 5,6,7,8-Tetrahydroquinoxaline
576. 5,7-Dihydro-2-Methylthieno(3,4-D)Pyrimidine
577. 5-Decenoic Acid
578. 5-Ethyl-2-Hydroxy-3-Methylcyclopent-2-En-1-One
579. 5-Ethyl-2-Methylpyridine
580. 5-Ethyl-3-Hydroxy-4-Methyl-2(5H)-Furanone
581. 5H-5-Methyl-6,7-Dihydrocyclopenta(B)Pyrazine
582. 5-Hydroxy-2,4-Decadienoic Acid Delta-Lactone
583. 5-Hydroxy-2-Decenoic Acid Delta-Lactone
584. 5-Hydroxy-2-Dodecenoic Acid Lactone
585. 5-Hydroxy-4-Octanone
586. 5-Hydroxy-7-Decenoic Acid Delta-Lactone
587. 5-Hydroxy-8-Undecenoic Acid Delta-Lactone
588. 5-Hydroxyundecanoic Acid Lactone
589. 5-Isopropenyl-2-Methyl-2-Vinyltetrahydrofuran
590. 5-Methyl-2,3-Hexanediol
591. 5-Methyl-2-Hepten-4-One
592. 5-Methyl-2-Phenyl-2-Hexenal
593. 5-Methyl-2-Thiophenecarboxaldehyde
594. 5-Methyl-3-Hexen-2-One
595. 5-Methyl-5-Hexen-2-One
596. 5-Methylfurfural
597. 5-Methylhexanoic Acid
598. 5-Methylquinoxaline
599. 5-Phenylpentanol
600. 6,7-Dihydro-2,3-Dimethyl-5H-Cyclopentapyrazine
601. 6-Acetoxydihydrotheaspirane
602. 6-Decenoic Acid
603. 6-Hydroxy-3,7-Dimethyloctanoic Acid Lactone
604. 6-Hydroxydihydrotheaspirane
605. 6-Methyl-3,5-Heptadien-2-One
606. 6-Methyl-3-Hepten-2-One, Trans-
607. 6-Methyl-5-Hepten-2-One
608. 6-Methyl-5-Hepten-2-One
609. 6-Methylcoumarin
610. 6-Methylquinoline
611. 6-Octenol
612. 7-Methyl-4,4a,5,6-Tetrahydro-2(3H)-Naphthalenone
613. 9,12-Octadecadienoic Acid (48%) And 9,12,15-Octadecatrienoic Acid
614. 9-Decenal
615. 9-Decenoic Acid
616. 9-Undecenal
617. Acacia, Gum (Acacia Senegal (L.) Willd.)
618. Acesulfame Potassium
619. Acetal
620. Acetaldehyde
621. Acetaldehyde Ethyl Cis-3-Hexenyl Acetal
622. Acetaldehyde Phenethyl Propyl Acetal
623. Acetaldehyde, Butyl Phenethyl Acetal
624. Acetanisole
625. Acetic Acid
626. Acetic Anhydride
627. Acetoin
628. Acetolein
629. Acetone
630. Acetone Peroxides
631. Acetophenone
632. Acetostearin
633. Acetyl Methyl Carbinyl Acetate
634. Acetylpyrazine
635. Aconitic Acid
636. Acrolein
637. Acrylamide-Acryl Acid Resin
638. Acrylamide-Sodium Acrylate Resin
639. Acrylic Acid-2-Acrylamido-2-Methyl Propane Sulfonic Acid Copolymer
640. Activated Carbon
641. Adipic Acid
642. Adipic Anhydride
643. Agar (Gelidium Spp.)
644. Albumin
645. Alcohol Sda-3A
646. Alcohol, Denatured Formula 23A
647. Alfalfa, Extract (Medicago Sativa L.)
648. Alfalfa, Herb And Seed (Medicago Sativa L.)
649. Algae, Brown, Extract (Macrocystis And Laminaria Spp.)
650. Algae, Red (Porphyra Spp. And Gloiopectis Furcata And Rhodymenia
651. Algae, Red, Extract (Porphyra Spp. And Gloiopectis Furcata And
652. Alginate, Ammonium
653. Alginate, Calcium
654. Alginate, Potassium
655. Alginate, Sodium
656. Alginate, Sodium Calcium
657. Alginic Acid
658. Alkanet Root, Extract (Alkanna Tinctoria Tausch)
659. Alkanolamide Of Coconut Oil Fatty Acids And Diethanolamine
660. Alkylene Oxide Adducts Of Alkyl Alcohols/Phosphate Esters Of Same,
661. Allspice (Pimenta Officinalis Lindl.)
662. Allspice, Oil (Pimenta Officinalis Lindl.)
663. Allspice, Oleoresin (Pimenta Officinalis Lindl.)
664. Allyl 10-Undecenoate
665. Allyl 2-Ethylbutyrate
666. Allyl 2-Furoate
667. Allyl Alpha-Ionone
668. Allyl Anthranilate
669. Allyl Butyrate
670. Allyl Cinnamate
671. Allyl Crotonate
672. Allyl Cyclohexaneacetate
673. Allyl Cyclohexanebutyrate
674. Allyl Cyclohexanehexanoate
675. Allyl Cyclohexanepropionate
676. Allyl Cyclohexanecarboxylic acid
677. Allyl Disulfide
678. Allyl Heptanoate
679. Allyl Hexanoate
680. Allyl Hexenoate
681. Allyl Isothiocyanate
682. Allyl Isovalerate
683. Allyl Mercaptan
684. Allyl Methyl Disulfide
685. Allyl Methyl Trisulfide
686. Allyl Nonanoate
687. Allyl Octanoate
688. Allyl Phenoxyacetate
689. Allyl Phenylacetate
690. Allyl Propionate
691. Allyl Sorbate
692. Allyl Sulfide
693. Allyl Thiopropionate
694. Allyl Tiglate
695. Almond, Bitter, Oil (Ffpa) (Prunus Spp.)
696. Aloe, Extract (Aloe Spp.)
697. Alpha-(P-(1,1,3,3-Tetramethylbutyl)Phenyl)-Omega-
Hydroxypoly(Oxyethylene)(1 Mol)
698. Alpha-(P-(1,1,3,3-Tetramethylbutyl)Phenyl)-Omega-
Hydroxypoly(Oxyethylene)(Greater Than 1 Mol)
699. Alpha-(P-Dodecylphenyl)-Omega-Hydroxypoly(Oxyethylene)
700. Alpha,Alpha-Dimethylbenzyl Isobutyrate
701. Alpha,Alpha-Dimethylphenethyl Acetate
702. Alpha,Alpha-Dimethylphenethyl Alcohol
703. Alpha,Alpha-Dimethylphenethyl Butyrate
704. Alpha,Alpha-Dimethylphenethyl Formate
705. Alpha-(P-(1,1,3,3-Tetramethylbutyl)Phenyl)-Omega-Hydroxypoly(Oxyethylene
706. Alpha-Acetolactate Decarboxylase Enzyme Preparation From Bacillus
707. Alpha-Alkyl-Omega-Hydroxy-Poly(Oxyethylene)
708. Alpha-Amylase Enzyme Preparation From Bacillus Stearothermophilus
709. Alpha-Amylcinnamaldehyde
710. Alpha-Amylcinnamaldehyde Dimethyl Acetal
711. Alpha-Amylcinnamyl Acetate
712. Alpha-Amylcinnamyl Alcohol
713. Alpha-Amylcinnamyl Formate
714. Alpha-Amylcinnamyl Isovalerate
715. Alpha-Butylcinnamaldehyde
716. Alpha-Butyl-Omega-Hydroxypoly(Oxyethylene) Poly(Oxypropylene)
717. Alpha-Campholenic Alcohol
718. Alpha-Damascone
719. Alpha-Ethyl Benzylo Butyrate
720. Alpha-Furfuryl Octanoate
721. Alpha-Furfuryl Pentanoate
722. Alpha-Galactosidase From Morteirella Vinaceae
723. Alpha-Hexylcinnamaldehyde
724. Alpha-Hydro-Omega-Hydroxypoly(Oxyethylene) Poly(Oxypropylene)
725. Alpha-Ionol
726. Alpha-Ionone
727. Alpha-Irone
728. Alpha-Isobutylphenethyl Alcohol
729. Alpha-Isomethylionone
730. Alpha-Isomethylionyl Acetate
731. Alpha-Ketobutyric Acid
732. Alpha-Methylbenzyl Acetate
733. Alpha-Methylbenzyl Alcohol
734. Alpha-Methylbenzyl Butyrate
735. Alpha-Methylbenzyl Formate
736. Alpha-Methylbenzyl Isobutyrate
737. Alpha-Methylbenzyl Propionate
738. Alpha-Methyl-Beta-Hydroxypropyl Alpha-Methyl-Beta-Mercaptopropyl
739. Alpha-Methylcinnamaldehyde
740. Alpha-Methylphenethyl Butyrate
741. Alpha-Pheillandrene
742. Alpha-Pinene
743. Alpha-Propylphenethyl Alcohol
744. Alpha-Terpinene
745. Alpha-Terpineol
746. Alpha-Terpinyl Anthranilate
747. Alpha-Tocopherol Acetate
748. Alpha-Tocopherol Acid Succinate
749. Althea Flowers (Althea Officinalis L.)
750. Althea Root (Althea Officinalis L.)
751. Alum (Double Sulfate Of Al And Nh4, K, Or Na)
752. Aluminum Ammonium Sulfate
753. Aluminum Calcium Silicate
754. Aluminum Caprate
755. Aluminum Caprylate
756. Aluminum Hydroxide
757. Aluminum Laurate
758. Aluminum Myristate
759. Aluminum Nicotinate
760. Aluminum Oleate
761. Aluminum Palmitate
762. Aluminum Potassium Sulfate
763. Aluminum Salts Of Fatty Acids
764. Aluminum Sodium Sulfate
765. Aluminum Stearate
766. Aluminum Sulfate
767. Ambergris, Tincture
768. Ambrette Seed (Hibiscus Abelmoschus L.)
769. Ambrette Seed, Oil (Hibiscus Abelmoschus L.)
770. Ambrette, Absolute, Oil (Hibiscus Abelmoschus L.)
771. Ambrette, Tincture (Hibiscus Abelmoschus L.)
772. Amino Tri(Methylene Phosphonic Acid), Sodium Salt
773. Aminoglycoside 3'-Phosphotransferase Ii
774. Aminopeptidase From Lactococcus Lactis
775. Ammonium Acetate
776. Ammonium Bicarbonate
777. Ammonium Carbonate
778. Ammonium Caseinate
779. Ammonium Chloride
780. Ammonium Citrate, Dibasic
781. Ammonium Gluconate
782. Ammonium Hydroxide
783. Ammonium Isovalerate
784. Ammonium Pectinate
785. Ammonium Persulfate
786. Ammonium Phosphate, Dibasic
787. Ammonium Phosphate, Monobasic
788. Ammonium Sulfate
789. Ammonium Sulfide
790. Ammonium Sulfite
791. Amyl 2-Furoate
792. Amyl Alcohol
793. Amyl Butyrate
794. Amyl Decanoate
795. Amyl Formate
796. Amyl Heptanoate
797. Amyl Hexanoate
798. Amyl Octanoate
799. Amyl Salicylate
800. Amylase From Aspergillus Flavus
801. Amylase From Aspergillus Niger
802. Amylase From Aspergillus Oryzae
803. Amylase From Bacillus Subtilis
804. Amyloglucosidase From Rhizopus Niveus
805. Amyris (Amyris Balsamifera L.)
806. Amyris, Oil (Amyris Balsamifera L.)
807. Angelica (Angelica Spp.)
808. Angelica Root (Angelica Spp.)
809. Angelica Root, Extract (Angelica Archangelica L.)
810. Angelica Root, Oil (Angelica Archangelica L.)
811. Angelica Seed (Angelica Spp.)
812. Angelica Seed, Extract (Angelica Archangelica L.)
813. Angelica Seed, Oil (Angelica Archangelica L.)
814. Angelica Stem, Oil (Angelica Archangelica L.)
815. Angola Weed (Roccella Fuciformis Ach.)
816. Angostura (Galiacea Officinalis Hancock)
817. Angostura, Extract (Galiacea Officinalis Hancock)
818. Anise (Pimpinella Anismus L.)
819. Anise, Oil (Pimpinella Anismus L.)
820. Anise, Star (Illicium Verum Hook, F.)
821. Anise, Star, Oil (Illicium Verum Hook, F.)
822. Anisic Acid
823. Anisole
824. Anisyl Acetate
825. Anisyl Alcohol
826. Anisyl Butyrate
827. Anisyl Formate
828. Anisyl Phenylacetate
829. Anisyl Propionate
830. Annatto, Extract (Bixa Orellana L.)
831. Annatto, Seed (Bixa Orellana L.)
832. Anoxomer
833. Anthracite Coal, Sulfonated
834. Apple Essence, Natural
835. Apricot Kernel, Oil (Prunus Armeniaca L.)
836. Arabinogalactan
837. Arnica Flowers (Arnica Spp.)
838. Arrowroot Starch
839. Artemisia (Artemisia Spp.)
840. Artemisia Extract
841. Artemisia Oil
842. Artichoke Leaves (Cynara Scolymus L.)
843. Asafetida, Fluid Extract (Ferula Assafoetida L.)
844. Asafetida, Gum (Ferula Assafoetida L.)
845. Asafetida, Oil (Ferula Assafoetida L.)
846. Ascorbic Acid
847. Ascorbyl Palmitate
848. Ascorbyl Stearate
849. Asparagus, Seed And Root, Extract
850. Aspartame
851. Aspergillus Niger For Fermentation Production Of Citric Acid
852. Astaxanthin
853. Azodicarbonamide
854. Bacterial Catalase From Micrococcus Lysodeikticus
855. Bakers Yeast Extract
856. Baker's Yeast Glycan
857. Baker's Yeast Protein
858. Balm (Melissa Officinalis L.)
859. Balm Leaves (Melissa Officinalis L.)
860. Balm Leaves, Extract (Melissa Officinalis L.)
861. Balm, Oil (Melissa Officinalis L.)
862. Balsam Fir, Oil (Abies Balsamea (L.) Mill.)
863. Balsam Fir, Oleoresin (Abies Balsamea (L.) Mill.)
864. Balsam, Peru (Myroxylon Pereirae Klotzsch)
865. Balsam, Peru, Oil (Myroxylon Pereirae Klotzsch)
866. Basil (Ocimum Basilicum L.)
867. Basil Bush (Ocimum Minimum L.)
868. Basil, Extract (Ocimum Basilicum L.)
869. Basil, Oil (Ocimum Basilicum L.)
870. Basil, Oleoresin (Ocimum Basilicum L.)
871. Bay (Laurus Nobilis L.)
872. Bay Leaves, Sweet, Extract (Laurus Nobilis L.)
873. Bay Leaves, Sweet, Oil (Laurus Nobilis L.)
874. Bay Leaves, West Indian, Extract (Pimenta Acris Kostel)
875. Bay Leaves, West Indian, Oil (Pimenta Racemosa (Mill.) J.W.
876. Bay Leaves, West Indian, Oleoresin (Pimenta Acris Kostel)
877. Beechwood, Creosote (Fagus Spp.)
878. Beeswax
879. Beeswax, Bleached
880. Bentonite
881. Benzaldehyde
882. Benzaldehyde Dimethyl Acetal
883. Benzaldehyde Glyceryl Acetal
884. Benzaldehyde Propylene Glycol Acetal
885. Benzene
886. Benzenethiol
887. Benzoic Acid
888. Benzoin
889. Benzoin, Resin (Styrax Spp.)
890. Benzophenone
891. Benzothiazole
892. Benzoyl Peroxide
893. Benzyl 2,3-Dimethylcrotonate
894. Benzyl Acetate
895. Benzyl Acetoacetate
896. Benzyl Alcohol
897. Benzyl Benzoate
898. Benzyl Butyl Ether
899. Benzyl Butyrate
900. Benzyl Cinnamate
901. Benzyl Disulfide
902. Benzyl Ethyl Ether
903. Benzyl Formate
904. Benzyl Isobutyrate
905. Benzyl Isovalerate
906. Benzyl Mercaptan
907. Benzyl Methoxyethyl Acetal
908. Benzyl Methyl Sulfide
909. Benzyl Phenylacetate
910. Benzyl Propionate
911. Benzyl Salicylate
912. Benzyl Trans-2-Methyl-2-Butenoate
913. Bergamot, Oil (Citrus Aurantium L. Subsp. Bergamia Wright Et Arn.)
914. Beta-Alanine
915. Beta-Apo-8'-Carotenal
916. Beta-Bourbonene
917. Beta-Carotene
918. Beta-Caryophyllene
919. Beta-Caryophyllene Alcohol
920. Beta-Caryophyllene Alcohol Acetate
921. Beta-Caryophyllene Oxide
922. Beta-Ionol
923. Beta-Ionone
924. Beta-Ionyl Acetate
925. Beta-Methylphenethyl Alcohol
926. Beta-Myrcene
927. Beta-Napthyl Anthranilate
928. Beta-Napthyl Ethyl Ether
929. Beta-Napthyl Isobutyl Ether
930. Beta-Napthyl Methyl Ether
931. Beta-Pinene
932. Beta-Terpineol
933. Biotin
934. Biphenyl
935. Birch Tar, Oil (Betula Pendula Roth And Related Betula Spp.)
936. Birch, Sweet, Oil (Betula Lenta L.)
937. Bis(2,5-Dimethyl-3-Furyl) Disulfide
938. Bis(2-Methyl-3-Furyl) Disulfide
939. Bis(2-Methyl-3-Furyl) Tetrasulfide
940. Bis-(Methylthio)Methane
941. Bisabolene
942. Blackberry Bark, Extract (Rubus, Spp. Of Section Eubatus)
943. Blackberry Fruit Extract
944. Bois De Rose, Oil (Aniba Rosaeodora Ducke)
945. Boldus Leaves (Peumus Boldus Mol.)
946. Bonito, Dried
947. Borax
948. Boric Acid
949. Borneol
950. Bornyl Acetate
951. Bornyl Butyrate
952. Bornyl Formate
953. Bornyl Isovalerate
954. Bornyl Valerate
955. Boronia, Absolute (Boronia Megastigma Nees)
956. Bouillon, Vegetable, Smoke
957. Bromelain
958. Brominated Vegetable Oil
959. Bryonia Root (Bryonia Spp.)
960. Buchu Leaves (Barosma Betulina And Crenulata)
961. Buchu Leaves Extract
962. Buchu Leaves, Oil (Barosma Spp.)
963. Buckbean Leaves (Menyanthes Trifoliata L.)
964. Buckbean Leaves, Extract (Menyanthes Trifoliata L.)
965. Butadiene-Styrene Rubber
966. Butan-3-One-2-Yl Butanoate
967. Butter Acids
968. Butter Esters
969. Butter Fat, Enzyme-Modified, With Added Butyric Acid
970. Butter Starter Distillate
971. Butyl 10-Undecenoate
972. Butyl 2-Decenoate
973. Butyl Acetate
974. Butyl Acetoacetate
975. Butyl Alcohol
976. Butyl Anthranilate
977. Butyl Butyrate
978. Butyl Butyrylactate
979. Butyl Cinnamate
980. Butyl Ethyl Malonate
981. Butyl Formate
982. Butyl Heptanoate
983. Butyl Hexanoate
984. Butyl Isobutyrate
985. Butyl Isovalerate
986. Butyl Lactate
987. Butyl Laurate
988. Butyl Levulinate
989. Butyl Oleate Sulfate
990. Butyl Phenylacetate
991. Butyl P-Hydroxybenzoate
992. Butyl Propionate
993. Butyl Salicylate
994. Butyl Stearate
995. Butyl Sulfide
996. Butyl Valerate
997. Butylamine
998. Butylated Hydroxyanisole
999. Butylated Hydroxytoluene
1000. Butyraldehyde
1001. Butyric Acid
1002. Cadinene
1003. Caffeine
1004. Cajeput, Oil (Melaleuca Leucadendron L.)
1005. Calamus Extract—Prohibited
1006. Calamus Oil—Prohibited
1007. Calamus—Prohibited
1008. Calcium Acetate
1009. Calcium Ascorbate
1010. Calcium Benzoate
1011. Calcium Bromate
1012. Calcium Caprate
1013. Calcium Caprylate
1014. Calcium Carbonate
1015. Calcium Caseinate
1016. Calcium Chloride
1017. Calcium Citrate
1018. Calcium Cyclamate—Prohibited
1019. Calcium Dibutylphosphate
1020. Calcium Fumarate
1021. Calcium Gluconate
1022. Calcium Glycerophosphate
1023. Calcium Hexametaphosphate
1024. Calcium Hydroxide
1025. Calcium Hypophosphite
1026. Calcium Iodate
1027. Calcium Lactate
1028. Calcium Lactobionate
1029. Calcium Laurate
1030. Calcium Lignosulfonate
1031. Calcium Myristate
1032. Calcium Oleate
1033. Calcium Oxide
1034. Calcium Palmitate
1035. Calcium Pantothenate
1036. Calcium Pantothenate, Calcium Chloride Double Salt
1037. Calcium Peroxide
1038. Calcium Phosphate, Dibasic
1039. Calcium Phosphate, Monobasic
1040. Calcium Phosphate, Tribasic
1041. Calcium Phytate
1042. Calcium Propionate
1043. Calcium Pyrophosphate
1044. Calcium Salts Of Fatty Acids
1045. Calcium Silicate
1046. Calcium Sorbate
1047. Calcium Stearate
1048. Calcium Stearoyl-2-Lactylate
1049. Calcium Sulfate
1050. Calumba Root (Jatropha Palmata (Lam.) Miers)
1051. Calumba Root, Extract (Jatropha Palmata (Lam.) Miers)
1052. Camphene
1053. Campholene Acetate
1054. Camphor Oil, Formosan Ho-Sho, Leaves (Cinnamomum Camphora)
1055. Camphor, Japanese, White, Oil (Cinnamomum Camphora (L.) Nees Et
1056. Cananga, Oil (Cananga Odorata Hook. F. And Thoms.)
1057. Candelilla Wax (Wax From Stems And Branches Of Euphorbia Cerifera)
1058. Candida Guillermondii
1059. Candida Lipolytica
1060. Canthaxanthin
1061. Capers (Capparis Spinosa L.)
1062. Capsicum (Capsicum Spp.)
1063. Capsicum Extract (Capsicum Spp.)
1064. Capsicum, Oleoresin (Capsicum Spp.)
1065. Caramel
1066. Caraway (Carum Carvi L.)
1067. Caraway, Black (Nigella Sativa L.)
1068. Caraway, Oil (Carum Carvi L.)
1069. Carbohydrase And Cellulase From Aspergillus Niger
1070. Carbohydrase And Protease, Mixture, From Bacillus Subtilis
1071. Carbohydrase From Aspergillus Oryzae
1072. Carbohydrase From Bacillus Amyloliquefaciens
1073. Carbohydrase From Bacillus Licheniformis
1074. Carbohydrase From Bacillus Subtilis
1075. Carbohydrase From Rhizopus Oryzae
1077. Carbohydrase/Proteinase Preparation, Bacillus Licheniformis
1078. Carbon Dioxide
1079. Carboxymethyl Cellulose
1080. Carboxymethyl Cellulose, Sodium Salt
1081. Carboxymethyl Hydroxyethyl Cellulose
1082. Cardamom (Elettaria Cardamomum (L.) Maton)
1083. Cardamom Oleoresin
1084. Cardamom Seed, Oil (Elettaria Cardamomum (L.) Maton)
1085. Carmine (Coccus Cacti L.)
1086. Carnauba Wax (Copernicia Cerifera (Arruda) Mart.)
1087. Carob Bean, Extract (Ceratonia Siliqua L.)
1088. Carrageenan
1089. Carrageenan And Salts Of Carrageenan
1090. Carrageenan Salts With Polysorbate 80
1091. Carrageenan With Polysorbate 80
1092. Carrageenan, Ammonium Salt Of
1093. Carrageenan, Ammonium Salt Of, With Polysorbate 80
1094. Carrageenan, Calcium Salt Of
1095. Carrageenan, Calcium Salt Of, With Polysorbate 80
1096. Carrageenan, Potassium Salt Of
1097. Carrageenan, Potassium Salt Of, With Polysorbate 80
1098. Carrageenan, Sodium Salt Of
1099. Carrageenan, Sodium Salt Of, With Polysorbate 80
1100. Carrot, Oil (Daucus Carota L.)
1101. Carvacrol
1102. Carvacryl Ethyl Ether
1103. Carveol
1104. Carvomenthol
1105. Carvone
1106. Carvyl Acetate
1107. Carvyl Propionate
1108. Caryophyllene Alcohol
1109. Caryophyllene Alcohol Acetate
1110. Cascara, Bitterless, Extract (Rhamnus Purshiana Dc.)
1111. Cascarilla Bark, Extract (Croton Spp.)
1112. Cascarilla Bark, Oil (Croton Spp.)
1113. Casein
1114. Cassia Buds (Cinnamomum Cassia Blume)
1115. Cassie, Absolute (Acacia Farnesiana (L.) Willd.)
1116. Castor Oil (Ricinus Communis L.)
1117. Castoreum, Extract (Castor Spp.)
1118. Castoreum, Liquid (Castor Spp.)
1119. Catalase From Aspergillus Niger
1120. Catalase From Bovine Liver
1121. Catalase From Penicillium Notatum
1122. Catechu, Black, Extract (Acacia Catechu Willd.)
1123. Catechu, Black, Powder (Acacia Catechu Willd.)
1124. Cedar Leaf, Oil (Thuja Occidentalis L.)
1125. Cedarwood Oil Alcohols
1126. Cedarwood Oil Terpenes
1127. Cedryl Acetate
1128. Celery Seed (Apium Graveolens L.)
1129. Celery Seed, Extract (Apium Graveolens L.)
1130. Celery Seed, Extract Solid (Apium Graveolens L.)
1131. Celery Seed, Oil (Apium Graveolens L.)
1132. Celery Seed, Oleoresin
1133. Cellulase From Trichoderma Longibrachiatum
1134. Cellulose Acetate
1135. Cellulose Triacetate
1136. Cellulose, Diethylaminoethyl
1137. Cellulose, Methyl
1138. Cellulose, Methyl Ethyl
1139. Cellulose, Microcrystalline
1140. Centaury (Centaurium Umbellatum Gilib.)
1141. Cereal Solids, Hydrolyzed
1142. Cetyl Alcohol
1143. Chamomile Flower (Anthemis Nobilis L.)
1144. Chamomile Flower (Matricaria Chamomilla L.)
1145. Chamomile Flower, Hungarian, Oil (Matricaria Chamomilla L.)
1146. Chamomile Flower, Oil (Anthemis Nobilis L.)
1147. Chamomile Flower, Roman, Extract (Anthemis Nobilis L.)
1148. Char Smoke Flavor
1149. Cherry Bark, Wild, Extract (Prunus Serotina Ehrh.)
1150. Cherry Laurel, Oil (Prunus Laurocerasus L.) (Ffpa)
1151. Cherry Pits, Extract (Prunus Spp.)
1152. Cherry-Laurel Leaves (Prunus Laurocerasus L.)
1153. Cherry-Laurel Water (Prunus Laurocerasus L.)
1154. Chervil (Anthriscus Cerefolium (L.) Hoffm.)
1155. Chervil, Extract (Anthriscus Cerefolium L.)
1156. Chestnut Leaves (Castanea Dentata (Marsh.) Borkh.)
1157. Chestnut Leaves, Extract (Castanea Dentata (Marsh.) Borkh.)
1158. Chestnut Leaves, Extract Solid (Castanea Dentata (Marsh.) Borkh.)
1159. Chicle (Manilkara Zapotilla Gilly And M. Chicle Gilly)
1160. Chicle, Venezuelian (Manilkara Williamsii Standley And Related
1161. Chicory, Extract (Cichorium Intybus L.)
1162. Chittle (Cnidoscolus (Also Known As Jatropha) Spp.)
1163. Chiquibul (Manilkara Zapotilla Gilly)
1164. Chirata (Swertia Chirata Buch.-Ham.)
1165. Chirata, Extract (Swertia Chirata Buch.-Ham.)
1166. Chives (Allium Schoenoprasum L.)
1167. Chlorine
1168. Chlorine Dioxide
1169. Chlorine Solution, Aqueous
1170. Chlorofluorocarbon 113
1171. Chlorofluorocarbons--Prohibited
1172. Chloroform
1173. Chloromethyl Methyl Ether
1174. Chloropentafluoroethane
1175. Chlorophyll
1176. Cholic Acid
1177. Choline Bitartrate
1178. Choline Chloride
1179. Chymosin Preparation, Aspergillus Niger Var. Awamori
1180. Chymosin Preparation, Escherichia Coli K-12
1181. Chymosin Preparation, Kluyveromyces Marxianus Var. Lactis
1182. Cinchona Bark, Red (Cinchona Succirubra Pav. Or Its Hybrids)
1183. Cinchona Bark, Red, Extract (Cinchona Succirubra Pav. Or Its
1184. Cinchona Bark, Yellow (Cinchona Spp.)
1185. Cinchona Bark, Yellow, Extract (Cinchona Spp.)
1186. Cinchona, Extract (Cinchona Spp.)
1187. Cinnamaldehyde
1188. Cinnamaldehyde Ethylene Glycol Acetal
1189. Cinnamic Acid
1190. Cinnamon (Cinnamomum Spp.)
1191. Cinnamon Bark Oleoresin, Ceylon, Chinese, Or Saigon (Cinnamomum
1192. Cinnamon Bark, Extract (Cinnamomum Spp.)
1193. Cinnamon Bark, Oil (Cinnamomum Spp.)
1194. Cinnamon Leaf Oil, Rectified
1195. Cinnamon Leaf, Oil (Cinnamomum Spp.)
1196. Cinnamyl Acetate
1197. Cinnamyl Alcohol
1198. Cinnamyl Anthranilate -- Prohibited
1199. Cinnamyl Benzoate
1200. Cinnamyl Butyrate
1201. Cinnamyl Cinnamate
1202. Cinnamyl Formate
1203. Cinnamyl Isobutyrate
1204. Cinnamyl Isovalerate
1205. Cinnamyl Phenylacetate
1206. Cinnamyl Propionate
1207. Cis- And Trans-P-1(7),8-Menthadien-2-Yl
1208. Cis-2-Nonen-1-OIl
1209. Cis-3 & Trans-2-Hexenyl Propionate
1210. Cis-3-Nonen-1-OI
1211. Cis-3-Hexen-1-YI Acetate
1212. Cis-3-Hexenal
1213. Cis-3-Hexenyl Benzoate
1214. Cis-3-Hexenyl Butyrate
1215. Cis-3-Hexenyl Cis-3-Hexenoate
1216. Cis-3-Hexenyl Formate
1217. Cis-3-Hexenyl Hexanoate
1218. Cis-3-Hexenyl Lactate
1219. Cis-3-Octen-1-OI
1220. Cis-4-Heptenal
1221. Cis-4-Hexenal
1222. Cis-5-Isopropenyl-Cis-2-Methylcyclopentan-1-Carboxaldehyde
1223. Cis-5-Octen-1-OI
1224. Cis-5-Octenal
1225. Cis-6-Nonen-1-OI
1226. Cis-6-Nonenal
1227. Cis-Carvone Oxide
1228. Cis-Dihydrocarvone
1229. Citral
1230. Citral Diethyl Acetal
1231. Citral Dimethyl Acetal
1232. Citral Propylene Glycol Acetal
1233. Citric Acid
1234. Citronella, Oil (Cymbopogon Nardus Rendle)
1235. Citronellal
1236. Citronelloxyacetaldehyde
1237. Citronellyl Acetate
1238. Citronellyl Butyrate
1239. Citronellyl Formate
1240. Citronellyl Isobutyrate
1241. Citronellyl Phenylacetate
1242. Citronellyl Propionate
1243. Citronellyl Valerate
1244. Citrus Peels, Extract (Citrus Spp.)
1245. Citrus Red No. 2
1246. Civet, Absolute (Viverra Civetta Schreber And Viverra Zibetha)
1247. Clary (Salvia Sclarea L.)
1248. Clary Sage, Absolute
1249. Clary Sage, Concrete
1250. Clary, Oil (Salvia Sclarea L.)
1251. Clay, Attapulgite
1252. Clove Bud, Extract (Eugenia Spp.)
1253. Clove Bud, Oil (Eugenia Spp.)
1254. Clove Bud, Oleoresin (Eugenia Spp.)
1255. Clove Leaf, Oil (Eugenia Spp.)
1256. Clove Stem, Oil (Eugenia Spp.)
1257. Clover (Trifolium Spp.)
1258. Clover Tops, Red, Extract Solid (Trifolium Pratense L.)
1259. Clover, Extract (Trifolium Spp.)
1260. Clover, Oil (Trifolium Spp.)
1261. Cloves (Eugenia Spp.)
1262. Cobalt Sulfate—Prohibited
1263. Cobaltous Chloride—Prohibited
1264. Coca Leaf, Extract (Decocainized) (Erythroxylon Coca Lam.)
1265. Cochineal Extract (Coccus Cacti L.)
1266. Cocoa Butter Substitute From Coconut Oil, Palm Kernel Oil Or
1267. Cocoa Butter Substitute From Palm Oil
1268. Cocoa Butter Substitute Primarily From High-Oleic Safflower Or
1269. Cocoa Extract
1270. Cocoa With Dioctyl Sodium Sulfosuccinate
1271. Coconut Oil
1272. Coconut Oil, Refined
1273. Coffee Concentrate, Pure
1274. Coffee Extract (Coffea Spp.)
1275. Coffee Extract, Solid
1276. Cognac, Green, Oil
1277. Cognac, White, Oil
1278. Collagen
1279. Combustion Product Gas
1280. Copaiba (South American Spp. Of Copaifera L.)
1281. Copaiba, Oil (South American Spp. Of Copaifera L.)
1282. Copals, Manila
1283. Copper Gluconate
1284. Copper Sulfate
1285. Coriander (Coriandrum Sativum L.)
1286. Coriander Leaf Oil (Coriandrum Sativum L.)
1287. Coriander, Oil (Coriandrum Sativum L.)
1288. Cork, Oak (Quercus Spp.)
1289. Corn Endosperm Oil
1290. Corn Gluten
1291. Corn Mint Oil
1292. Corn Silk
1293. Corn Silk Extract (Zea Mays L.)
1294. Corn Silk, Oil (Zea Mays L.)
1295. Corn Steep Liquor
1296. Corn Syrup
1297. Cornstarch
1298. Cornstarch, Waxy
1299. Costmary (Chrysanthemum Balsamita L.)
1300. Costus Root, Oil (Saussurea Lappa Clarke)
1301. Cottonseed Flour, Defatted
1302. Cottonseed Flour, Partially Defatted, Cooked
1303. Cottonseed Flour, Partially Defatted, Cooked, Toasted
1304. Cottonseed Kernels, Glandless, Raw
1305. Cottonseed Kernels, Glandless, Roasted
1306. Coumarin—Prohibited
1307. Coumarone-Indene Resins
1308. Crown Gum
1309. Cubeb (Piper Cubeba L. F.)
1310. Cubeb, Oil (Piper Cubeba L. F.)
1311. Cumin (Cuminum Cyminum L.)
1312. Cumin, Oil (Cuminum Cyminum L.)
1313. Cuminaldehyde
1314. Cuprous Iodide
1315. Curdian
1316. Currant Buds, Black, Absolute (Ribes Nigrum L.)
1317. Currant Juice, Black
1318. Currant Leaves, Black (Ribes Nigrum L.)
1319. Cyclamate—Prohibited
1320. Cycloheptadeca-9-En-1-One
1321. Cyclohexane
1322. Cyclohexaneacetic Acid
1323. Cyclohexanecarboxylic Acid
1324. Cyclohexaneethyl Acetate
1325. Cyclohexyl Acetate
1326. Cyclohexyl Anthranilate
1327. Cyclohexyl Butyrate
1328. Cyclohexyl Cinnamate
1329. Cyclohexyl Formate
1330. Cyclohexyl Isovalerate
1331. Cyclohexyl Propionate
1332. Cyclohexylamine
1333. Cyclohexylmethyl Pyrazine
1334. Cycloionone
1335. Cyclopentanethiol
1336. Cyclopentanone
1337. Daidai Peel Oil
1338. Damar Gum (Shorea Dipterocarpaceae)
1339. Damiana Leaves (Turnera Diffusa Wild.)
1340. Dandelion Root, Extract Solid (Taraxacum Spp.)
1341. Dandelion, Fluid Extract (Taraxacum Spp.)
1342. Davana Oil (Artemesia Pallens Wall.)
1343. D-Camphor
1344. Decanal
1345. Decanal Dimethyl Acetal
1346. Decanoic Acid
1347. Decyl Acetate
1348. Decyl Butyrate
1349. Decyl Propionate
1350. Deertongue Solid Extract
1351. Dehydrated Beets
1352. Dehydroacetic Acid
1353. Dehydrodihydroionol
1354. Dehydrodihydroionone
1355. Dehydrromenthofurolactone
1356. Delta-Damascone
1357. Delta-Decalactone
1358. Delta-Dodecalactone
1359. Delta-Hexalactone
1360. Delta-Octalactone
1361. Delta-Tetradecalactone
1362. Desoxycholic Acid
1363. Dextran (Avg M W Less Than 100,000)
1364. Dextrin
1365. Dextrose
1366. D-Fenchone
1367. D-Gluconic Acid
1368. Di-((Butan-3-One-1-Yl) Sulfide
1369. Diacetyl
1370. Diallyl Polysulfides
1371. Diallyl Trisulfide
1372. Diamyl Ketone
1373. Diastase From Aspergillus Oryzae
1374. Diatomaceous Earth
1375. Dibenzyl Ether
1376. Dibutyl Sebacate
1377. Dichlorodifluoromethane
1378. Dicyclohexyl Disulfide
1379. Diethanolamide Condensate From Soybean Oil Fatty Acids (C16-C18)
1380. Diethanolamide Condensate From Stripped Coconut Oil Fatty
1381. Diethyl Malate
1382. Diethyl Malonate
1383. Diethyl Pyrocarbonate -- Prohibited
1384. Diethyl Sebacate
1385. Diethyl Succinate
1386. Diethyl Sulfide
1387. Diethyl Tartrate
1388. Diethylaminoethanol
1389. Diethylene Glycol Distearate
1390. Diethylenetriamine
1391. Diethylenetriamine Crosslinked With Epichlorohydrin
1392. Difurfuryl Ether
1393. Dihydro-2,4,6-Trimethyl-4H-1,3,5-Dithiazine
1394. Dihydro-2,4,6-Tris(2-Methylpropyl)-4H-1,3,5-Dithiazine
1395. Dihydro-Alpha-Ionone

SUBSTITUTE SHEET (RULE 26)
1396. Dihydro-Beta-ionol
1397. Dihydro-Beta-ionone
1398. Dihydrocarveol
1399. Dihydrocarvyl Acetate
1400. Dihydrocoumarin
1401. Dihydronootkatone
1402. Dihydroxyacetophenone
1403. Diisobutyl Ketone
1404. Diisopropyl Disulfide
1405. Diisopropyl Trisulfide
1406. Dilauryl Thiodipropionate
1407. Dill (Anethum Graveolens L.)
1408. Dill Seed Oil (Anethum Sowa Roxb.)
1409. Dill Seed, Indian (Anethum Spp.)
1410. Dill, Oil (Anethum Graveolens L.)
1411. Dimethyl Dialkyl Ammonium Chloride
1412. Dimethyl Dicarbonate
1413. Dimethyl Succinate
1414. Dimethyl Trisulfide
1415. Dimethylamine
1416. Dimethylamine-Epichlorohydrin Copolymer
1417. Dimethylethanolamine
1418. Dimethylpolysiloxane
1419. Di-N-Alkyl(C8-C18 From Coconut Oil) Dimethyl Ammonium Chloride
1420. Dioctyl Sodium Sulfosuccinate
1421. Diphenyl Ether
1422. Dipotassium Phosphate
1423. Dipropyl Trisulfide
1424. Disodium Citrate
1425. Disodium Cyanodithioimidocarbonate
1426. Disodium Ethylenediamine carbonate
1427. Disodium Guanilate
1428. Disodium Inosinate
1429. Disodium Succinate
1430. Dittany (Fraxinella) Roots (Dictamnus Albus L.)
1431. Dittany Of Crete (Origanum Dictamnus L.)
1432. DI-(3-Amino-3-Carboxypropyl)Dimethylsulfonium Chloride
1433. DI-Alanine
1434. DI-Citronellol
1435. DI-Cystine
1436. D-Limonene
1437. DI-Isoleucine
1438. DI-Isomethone
1439. DI-Limonene
1440. DI-Methionine
1441. DI-Phenylalanine
1442. DI-Valine
1443. D-Neomenthol
1444. Dodecyl Gallate
1445. Dodecyl Isobutyrate
1446. Dog Grass, Extract (Agropyron Repens (L.) Beauv.)
1447. D-Pantothenamide
1448. D-Pantothenyl Alcohol
1449. D-Piperitone
1450. Dragon's Blood, Extract (Daemonorops Spp. Or Other
1451. D-Ribose
1452. Dried Algae Meal
1453. D-Sorbitol
1454. Dulcin--Prohibited
1455. D-Xylose
1456. Edta, Calcium Disodium
1457. Edta, Disodium
1458. Edta, Disodium Iron
1459. Edta, Tetrasodium
1460. Egg White Lysozyme
1461. Elder Flowers (Sambucus Canadensis L. Or Sambucus Nigra L.)
1462. Elder Flowers, Extract (Sambucus Canadensis L. Or Sambucus Nigra L.)
1463. Elder Tree Leaves (Sambucus Nigra L.)
1464. Elecampane Root, Extract (Inula Helenium L.)
1465. Elecampane Root, Oil (Inula Helenium L.)
1466. Elemi, Gum
1467. Elemi, Oil (Canarium Spp.)
1468. Enzyme-Modified Fats
1469. Enzymes, Bacterial
1470. Enzymes, Proteolytic
1471. Epichlorohydrin
1472. Epichlorohydrin Crosslinked With Ammonia
1473. Epsilon-Decalactone
1474. Epsilon-Dodecalactone
1475. Erigeron, Oil (Erigeron Canadensis L.)
1476. Erythorbic Acid
1477. Esterase-Lipase From Mucor Miehei
1478. Estragole
1479. Ethanesulfonic Acid, 2-{1-{(Difluoro-((Trifluoroethenyl))O
1480. Ethoxyquin
1481. Ethyl (P-Tolylxoy)Acetate
1482. Ethyl 10-Undecenoate
1483. Ethyl 2-(Methylidithio)Propionate
1484. Ethyl 2-(Methylthio)Acetate
1485. Ethyl 2,4,7-Decatrienoate
1486. Ethyl 2,4-Dioxohexanoate
1487. Ethyl 2-Acetyl-3-Phenylpropionate
1488. Ethyl 2-Ethyl-3-Phenylpropanoate
1489. Ethyl 2-Furanpropionate
1490. Ethyl 2-Hexenoate
1491. Ethyl 2-Mercaptopropionate
1492. Ethyl 2-Methyl-3,4-Pentadienoate
1493. Ethyl 2-Methyl-3-Pentenoate
1494. Ethyl 2-Methyl-4-Pentenoate
1495. Ethyl 2-Methylbutyrate
1496. Ethyl 2-Methylpentanoate
1497. Ethyl 2-Nonynoate
1498. Ethyl 3-(Furfurylthio) Propionate
1499. Ethyl 3-(Methylthio)Butyrate
1500. Ethyl 3-Hexenoate
1501. Ethyl 3-Hydroxybutyrate
1502. Ethyl 3-Hydroxyhexanoate
1503. Ethyl 3-Mercaptobutyrate
1504. Ethyl 3-Mercaptopropionate
1505. Ethyl 3-Methylpentanoate
1506. Ethyl 3-Methylthiopropionate
1507. Ethyl 3-Oxohexanoate
1508. Ethyl 3-Phenylglycidate
1509. Ethyl 3-Phenylpropionate
1510. Ethyl 4-(Acetyltio)Butyrate
1511. Ethyl 4-(Methylthio) Butyrate
1512. Ethyl 4-Heptenoate, Cis-
1513. Ethyl 4-Phenylbutyrate
1514. Ethyl 5-(Methylthio)Valerate
1515. Ethyl 5-Hexenoate
1516. Ethyl Abietate
1517. Ethyl Acetate
1518. Ethyl Acetoacetate
1519. Ethyl Aconitate (Mixed Esters)
1520. Ethyl Acrylate
1521. Ethyl Alcohol
1522. Ethyl Anthranilate
1523. Ethyl Benzoate
1524. Ethyl Benzoylacetaet
1525. Ethyl Brassylate
1526. Ethyl Butyrate
1527. Ethyl Cellulose
1528. Ethyl Cinnamate
1529. Ethyl Cis-4,7-Octadienoate
1530. Ethyl Cis-4-Octenoate
1531. Ethyl Crotonate
1532. Ethyl Cyclohexanecarboxylate
1533. Ethyl Cyclohexanopropionate
1534. Ethyl Decanoate
1535. Ethyl Esters Of Fatty Acids (Edible)
1536. Ethyl Formate
1537. Ethyl Heptanoate
1538. Ethyl Hexanoate
1539. Ethyl Isobutyrate
1540. Ethyl Isovalerate
1541. Ethyl Lactate
1542. Ethyl Laurate
1543. Ethyl Levulinate
1544. Ethyl Maltol
1545. Ethyl Methyl-P-Tolylglycidate
1546. Ethyl Myristate
1547. Ethyl N-Ethylanthranilate
1548. Ethyl Nitrite
1549. Ethyl Nonanoate
1550. Ethyl Octadecanoate
1551. Ethyl Octanoate
1552. Ethyl Oleate
1553. Ethyl Palmitate
1554. Ethyl P-Anisate
1555. Ethyl Phenylacetate
1556. Ethyl Propionate
1557. Ethyl Pyruvate
1558. Ethyl Salicylate
1559. Ethyl Sorbate
1560. Ethyl Thioacetate
1561. Ethyl Tiglate
1562. Ethyl Trans-2, Cis-4-Decadienoate
1563. Ethyl Trans-2-Decenoate
1564. Ethyl Trans-2-Hexenoate
1565. Ethyl Trans-2-Octenoate
1566. Ethyl Trans-4-Decenoate
1567. Ethyl Undecanoate
1568. Ethyl Valerate
1569. Ethyl Vanillin
1570. Ethyl Vanillin Beta-D-Glucopyranoside
1571. Ethyl Vanillin Isobutyrate
1572. Ethyl Vanillin Propylene Glycol Acetal
1573. Ethylene Dichloride
1574. Ethylene Glycol Distearate
1575. Ethylene Glycol Monobutyl Ether
1576. Ethylene Glycol Monoethyl Ether
1577. Ethylene Oxide
1578. Ethylene Oxide Polymer
1579. Ethylene Oxide Polymer, Alkyl Adduct
1580. Ethylene Oxide Polymer, Alkyl Adduct, Phosphate Ester
1581. Ethylene Oxide/Propylene Oxide Copolymer
1582. Ethylene Oxide/Propylene Oxide Copolymer (Avg M W 14,000)
1583. Ethylene Oxide/Propylene Oxide Copolymer (Avg M W 3,500-4,125)
1584. Ethylene Oxide/Propylene Oxide Copolymer (Avg M W 9,760 - 13,200)
1585. Ethylene Oxide/Propylene Oxide Copolymer (Min Avg M W 1,900)
1586. Ethylene Oxide/Propylene Oxide Copolymer, Alkyl Adduct
1587. Ethylene Oxide/Propylene Oxide Copolymer, Alkyl Adduct, Phosphate
1588. Ethylenediamine
1589. Eucalyptol
1590. Eucalyptus, Oil (Eucalyptus Globulus Labille)
1591. Eugenol
1592. Eugenyl Acetate
1593. Eugenyl Benzoate
1594. Eugenyl Formate
1595. Eugenyl Methyl Ether
1596. Farnesal
1597. Farnesene
1598. Farnesol
1599. Fatty Acids
1600. Fatty Alcohols, Synthetic
1601. FD&C Blue No. 1
1602. FD&C Blue No. 1, Aluminum Lake
1603. FD&C Blue No. 1, Calcium Lake
1604. FD&C Blue No. 2
1605. FD&C Blue No. 2, Aluminum Lake
1606. FD&C Blue No. 2, Calcium Lake
1607. FD&C Green No. 1--Prohibited
1608. FD&C Green No. 2--Prohibited
1609. FD&C Green No. 3
1610. FD&C Green No. 3, Aluminum Lake
1611. FD&C Green No. 3, Calcium Lake
1612. FD&C Red No. 1--Prohibited
1613. FD&C Red No. 2--Prohibited
1614. FD&C Red No. 3
1615. FD&C Red No. 3, Aluminum Lake--Prohibited
1616. FD&C Red No. 3, Calcium Lake--Prohibited
1617. FD&C Red No. 40
1618. FD&C Red No. 40, Aluminum Lake
1619. FD&C Red No. 40, Calcium Lake
1620. FD&C Red No. 4--Prohibited
1621. FD&C Violet No. 1--Prohibited
1622. FD&C Yellow No. 5
1623. FD&C Yellow No. 5, Aluminum Lake
1624. FD&C Yellow No. 5, Calcium Lake
1625. FD&C Yellow No. 6
1626. FD&C Yellow No. 6, Aluminum Lake
1627. FD&C Yellow No. 6, Calcium Lake
1628. Fenchyl Alcohol
1629. Fennel, Common (Foeniculum Vulgare Mill.)
1630. Fennel, Sweet (Foeniculum Vulgare Mill. Var. Dulce (D.C.) Alef.)
1631. Fennel, Sweet, Oil (Foeniculum Vulgare Mill. Var. Dulce (D.C.)
1632. Fenugreek (Trigonella Foenum-Graecum L.)
1633. Fenugreek, Extract (Trigonella Foenum-Graecum L.)
1634. Fenugreek, Oleoresin (Trigonella Foenum-Graecum L.)
1635. Ferric Ammonium Citrate, Brown
1636. Ferric Ammonium Citrate, Green
1637. Ferric Chloride
1638. Ferric Citrate
1639. Ferric Oxide
1640. Ferric Peptonate
1641. Ferric Phosphate
1642. Ferric Pyrophosphate
1643. Ferric Sodium Pyrophosphate
1644. Ferric Sulfate
1645. Ferrocyanide Salts
1646. Ferrous Ascorbate
1647. Ferrous Carbonate
1648. Ferrous Citrate
1649. Ferrous Fumarate
1650. Ferrous Gluconate
1651. Ferrous Lactate
1652. Ferrous Peptonate
1653. Ferrous Sulfate
1654. Ficin
1655. Fir ("Pine") Needles And Twigs (Abies Sibirica Ledeb.)
1656. Fir Needles And Twigs, Oil (Abies Spp.)
1657. Fir, Balsam, Needles And Twigs (Abies Balsamea (L.) Mill.)
1658. Fish Oil (Hydrogenated)
1659. Fish Protein Concentrate, Whole
1660. Fish Protein Isolate
1661. Folic Acid
1662. Formaldehyde
1663. Formic Acid
1664. Fruit Juice
1665. Fullers Earth
1666. Fumaric Acid
1667. Fungal Hemicellulase
1668. Fungal Pectinase
1669. Furcelleran
1670. Furcelleran And Salts Of Furcelleran
1671. Furcelleran, Ammonium Salt Of
1672. Furcelleran, Calcium Salt Of
1673. Furcelleran, Potassium Salt Of
1674. Furcelleran, Sodium Salt Of
1675. Furfural
1676. Furfuryl 3-Methylbutanoate
1677. Furfuryl Acetate
1678. Furfuryl Alcohol
1679. Furfuryl Butyrate
1680. Furfuryl Isopropyl Sulfide
1681. Furfuryl Mercaptan
1682. Furfuryl Methyl Ether
1683. Furfuryl Methyl Sulfide
1684. Furfuryl Propionate
1685. Furfuryl Propyl Disulfide
1686. Furfuryl Thioacetate
1687. Furfuryl Thiopropionate
1688. Fusel Oil, Refined
1689. Galanga, Greater (Alpinia Galanga Willd)
1690. Galangal Root (Alpinia Spp.)
1691. Galangal Root, Extract (Alpinia Spp.)
1692. Galangal Root, Oil (Alpinia Spp.)
1693. Galbanum, Oil (Ferula Spp.)
1694. Galbanum, Resin (Ferula Spp.)
1695. Gambir (Uncaria Gambir Roxb.)
1696. Gamma-Decalactone
1697. Gamma-Dodecalactone
1698. Gamma-Heptalactone
1699. Gamma-Hexalactone
1700. Gamma-Ionone
1701. Gamma-Methyldecalactone
1702. Gamma-Nonalactone
1703. Gamma-Octalactone
1704. Gamma-Terpinene
1705. Gamma-Undecalactone
1706. Gamma-Valerolactone
1707. Garlic
1708. Garlic Extract
1709. Garlic, Oil (Allium Sativum L.)
1710. Gelatin
1711. Gellan Gum
1712. Genet, Absolute (Spartium Junceum L.)
1713. Genet, Extract (Spartium Junceum L.)
1714. Gentian Root, Extract (Gentiana Lutea L.)
1715. Gentian, Stemless (Gentiana Acaulis L.)
1716. Geraniol
1717. Geranium (Pelargonium Spp.)
1718. Geranium Extract (Pelargonium Spp.)
1719. Geranium, East Indian, Extract (Cymbopogon Martini Stapf.)
1720. Geranium, East Indian, Oil (Cymbopogon Martini Stapf.)
1721. Geranium, Oil (Pelargonium Spp.)
1722. Geranium, Rose, Oil (Pelargonium Graveolens L'her.)
1723. Geranyl Acetate
1724. Geranyl Acetoacetate
1725. Geranyl Acetone
1726. Geranyl Benzoate
1727. Geranyl Butyrate
1728. Geranyl Formate
1729. Geranyl Hexanoate
1730. Geranyl Isobutyrate
1731. Geranyl Isovalerate
1732. Geranyl Phenylacetate
1733. Geranyl Propionate
1734. Germander, Chamaedrys (Teucrum Chamaedrys L.)
1735. Germander, Chamaedrys, Extract (Teucrium Chamaedrys L.)
1736. Germander, Chamaedrys, Extract Solid (Teucrium Chamaedrys L.)
1737. Germander, Golden (Teucum Polium L.)
1738. Ghatti, Gum (Anogeissus Latifolia Wall.)
1739. Gibberellic Acid & Potassium Gibberellate
1740. Ginger (Zingiber Officinale Rosc.)
1741. Ginger, Extract (Zingiber Officinale Rosc.)
1742. Ginger, Oil (Zingiber Officinale Rosc.)
1743. Ginger, Oleoresin (Zingiber Officinale Rosc.)
1744. Glucono-Delta Lactone
1745. Glucose Isomerase From Bacillus Coagulans
1746. Glucose Isomerase From Immobilized Arthrobacter Globiformis
1747. Glucose Isomerase From Streptomyces Olivaceus
1748. Glucose Isomerase From Streptomyces Olivochromogenes
1749. Glucose Isomerase From Streptomyces Rubiginosus
1750. Glucose Oxidase Catalase Preparation
1751. Glucose Oxidase From Aspergillus Niger
1752. Glucose Oxidase From Penicillium Notatum
1753. Glucose Pentaacetate
1754. Glucosidase From Aspergillus Flavus
1755. Glucosidase From Aspergillus Niger
1756. Glucosidase From Aspergillus Oryzae
1757. Glutamic Acid Hydrochloride
1758. Glutaraldehyde
1759. Gluten, Gum
1760. Glycerin
1761. Glycerin, Synthetic
1762. Glycerol Tributyrate
1763. Glycerol 5-Hydroxydecanoate
1764. Glycerol 5-Hydroxydodecanoate
1765. Glycerol Behenate
1766. Glycerol Lactooleate
1767. Glycerol Lactopalmitate
1768. Glycerol Monooleate
1769. Glycerol Monostearate
1770. Glycerol Palmitostearate
1771. Glycerol Tribenzoate
1772. Glycerol Tripropanoate
1773. Glycerol Tristearate
1774. Glycerol-Lacto Esters Of Fatty Acids
1775. Glycine
1776. Glycocalcic Acid
1777. Glycyrrhizin, Ammoniated (Glycyrrhiza Spp.)
1778. Grains Of Paradise (Aframomum Melegueta (Rosc.) K. Schum.)
1779. Grape Color Extract
1780. Grape Essence, Natural
1781. Grape Skin Extract
1782. Grapefruit Essence, Natural
1783. Grapefruit Oil, Conc.
1784. Grapefruit, Extract
1785. Grapefruit, Juice
1786. Grapefruit, Oil (Citrus Paradisi Macf.)
1787. Grapefruit, Oil, Terpeneless (Citrus Paradisi)
1788. Ground Limestone
1789. Guaiac Gum (Guaiacum Spp.)
1790. Guaiac Gum, Extract (Guaiacum Spp.)
1791. Guaiac Wood, Extract (Guaiacum Spp.)
1792. Guaiac Wood, Oil (Guaiacum Spp.)
1793. Guaiacol
1794. Guaiacyl Acetate
1795. Guaiacyl Phenylacetate
1796. Guaiene
1797. Guaiol Acetate
1798. Guar, Gum (Cyamopsis Tetragonolobus (L.))
1799. Guarana Seed, Extract
1800. Guarana, Gum (Paullinia Cupana Hbk)
1801. Guava (Psidium Spp.)
1802. Guava Extract
1803. GUTTA HANG KANG (Palaquium Reiocarpum Boerl. And P.
1804. Haematococcus Algae Meal
1805. Haw Bark, Black, Extract (Viburnum Prunifolium L.)
1806. Helium
1807. Hemlock (Tsuga Spp.)
1808. Hemlock Needles And Twigs, Oil (Tsuga Spp.)
1809. Heptanal
1810. Heptanal Dimethyl Acetal
1811. Heptanal Glyceryl Acetal (Mixed 1,2 And 1,3 Acetals)
1812. Heptanoic Acid
1813. Heptyl Acetate
1814. Heptyl Alcohol
1815. Heptyl Butyrate
1816. Heptyl Cinnamate
1817. Heptyl Formate
1818. Heptyl Isobutyrate
1819. Heptyl Octanoate
1820. Heptylparaben
1821. Hesperidin
1822. Hexanal
1823. Hexane
1824. Hexanoic Acid
1825. Hexyl 2-Furoate
1826. Hexyl 2-Methyl-3(Or 4)-Pentenoate
1827. Hexyl 2-Methylbutyrate
1828. Hexyl Acetate
1829. Hexyl Alcohol
1830. Hexyl Benzoate
1831. Hexyl Butyrate
1832. Hexyl Formate
1833. Hexyl Hexanoate
1834. Hexyl Isobutyrate
1835. Hexyl Isonovalerate
1836. Hexyl Octanoate
1837. Hexyl Phenylacetate
1838. Hexyl Propionate
1839. Hexyl Trans-2-Hexenoate
1840. Hickory Bark, Extract (Carya Spp.)
1841. Hickory Smoke Dist.
1842. High Fructose Corn Syrup
1843. Home | About | Search
1844. Hops Extract, Modified
1845. Hops, Extract (Humulus Lupulus L.)
1846. Hops, Extract Solid (Humulus Lupulus L.)
1847. Hops, Oil (Humulus Lupulus L.)
1848. Horehound (Marrubium Vulgare L.)
1849. Horehound Extract (Marrubium Vulgare L.)
1850. Horehound Solid, Extract
1851. Horsemint Leaves, Extract (Monarda Spp.)
1852. Horseradish (Armoracia Lapatiffolia Gilib.)
1853. Horseradish Oil
1854. Hyacinth Flowers (Hyacinthus Orientalis L.)
1855. Hyacinth, Absolute (Hyacinthus Orientalis L.)
1856. Hydratropic Aldehyde Propylene Glycol Acetal
1857. Hydrazine
1858. Hydrochloric Acid
1859. Hydrogen Peroxide
1860. Hydrogen Sulfide
1861. Hydroquinone Monoethyl Ether
1862. Hydroxyceitronellal
1863. Hydroxyceitronellal Diethyl Acetal
1864. Hydroxyceitronellal Dimethyl Acetal
1865. Hydroxyceitronellol
1866. Hydroxylated Lecithin
1867. Hydroxyxynonanoic Acid, Delta-Lactone
1868. Hydroxypropyl Cellulose
1869. Hydroxypropyl Methylcellulose
1870. Hyssop (Hyssopus Officinalis L.)
1871. Hyssop, Extract (Hyssopus Officinalis L.)
1872. Hyssop, Oil (Hyssopus Officinalis L.)
1873. Iceland Moss (Cetraria Islandica Ach.)
1874. Immortelle, Absolute (Helichrysum Angustifolium Dc.)
1875. Immortelle, Extract (Helichrysum Angustifolium Dc.)
1876. Imperatoria (Peucedanum Ostruthium (L.) Koch (Imperatoria Ostruthium
1877. Indole
1878. Inositol
1879. Insoluble Glucose Isomerase Enzyme Preparations
1880. Invert Sugar
1881. Invert Sugar Syrup
1882. Invertase From Saccharomyces Cerevisiae
1883. Ion Exchange Membranes
1884. Ion Exchange Resin
1885. Iron Ammonium Citrate
1886. Iron Caprylate
1887. Iron Citrate
1888. Iron Linoleate
1889. Iron Naphthenate
1890. Iron Oxide
1891. Iron Peptonate
1892. Iron Polyvinylpyrrolidone
1893. Iron Tallate
1894. Iron, Elemental
1895. Iron-Choline Citrate Complex
1896. Isoamyl 2-Methylbutyrate
1897. Isoamyl 3-(2-Furan)Propionate
1898. Isoamyl 4-(2-Furan)Butyrate
1899. Isoamyl Acetate
1900. Isoamyl Acetoacetate
1901. Isoamyl Alcohol
1902. Isoamyl Benzoate
1903. Isoamyl Butyrate
1904. Isoamyl Cinnamate
1905. Isoamyl Formate
1906. Isoamyl Hexanoate
1907. Isoamyl Isobutyrate
1908. Isoamyl Isovalerate
1909. Isoamyl Laurate
1910. Isoamyl Nonanoate
1911. Isoamyl Octanoate
1912. Isoamyl Phenylacetate
1913. Isoamyl Propionate
1914. Isoamyl Pyruvate
1915. Isoamyl Salicylate
1916. Isoborneol
1917. Isobornyl Acetate
1918. Isobornyl Formate
1919. Isobornyl Isovalerate
1920. Isobornyl Propionate
1921. Isobutane
1922. Isobutyl 2-Butenoate
1923. Isobutyl 2-Furanpropionate
1924. Isobutyl Acetate
1925. Isobutyl Acetoacetate
1926. Isobutyl Alcohol
1927. Isobutyl Angelate
1928. Isobutyl Anthranilate
1929. Isobutyl Benzoate
1930. Isobutyl Butyrate
1931. Isobutyl Cinnamate
1932. Isobutyl Formate
1933. Isobutyl Heptanoate
1934. Isobutyl Hexanoate
1935. Isobutyl Isobutyrate
1936. Isobutyl N-Methylantranilate
1937. Isobutyl Phenylacetate
1938. Isobutyl Propionate
1939. Isobutyl Salicylate
1940. Isobutylene-Isoprene Copolymer
1941. Isobutyrinaldehyde
1942. Isobutyric Acid
1943. Isocyclicitrals
1944. Isoeugenol
1945. Isoeugenyl Acetate
1946. Isoeugenyl Benzyl Ether
1947. Isoeugenyl Ethyl Ether
1948. Isoeugenyl Formate
1949. Isoeugenyl Methyl Ether
1950. Isoeugenyl Phenylacetate
1951. Isojasmine
1952. Isoparaffinic Petroleum Hydrocarbons, Synthetic
1953. Isopentylamine
1954. Isopentylideneisopentylamine
1955. Isophorone
1956. Isopropenylpyrazine
1957. Isopropyl 2-Methylbutyrate
1958. Isopropyl Acetate
1959. Isopropyl Alcohol
1960. Isopropyl Benzoate
1961. Isopropyl Butyrate
1962. Isopropyl Cinnamate
1963. Isopropyl Citrate
1964. Isopropyl Formate
1965. Isopropyl Hexanoate
1966. Isopropyl Isobutyrate
1967. Isopropyl Isovalerate
1968. Isopropyl Myristate
1969. Isopropyl Palmitate
1970. Isopropyl Phenylacetate
1971. Isopropyl Propionate
1972. Isopropyl Tiglate
1973. Isopropyl-2-Cyclohexenone
1974. Isopulegol
1975. Isopulegone
1976. Isopulegyl Acetate
1977. Isoquinoline
1978. Isovaleric Acid
1979. Iva (Achillea Moschata Jacq.)
1980. Iva, Extract (Achillea Moschata Jacq.)
1981. Jambu Oleoresin
1982. Japan Wax
1983. Jasmine, Absolute (Jasminum Spp.)
1984. Jasmine, Concrete (Jasminum Spp.)
1985. Jasmine, Oil (Jasminum Grandiflorum L.)
1986. Jasmine, Spiritus (Jasminum Grandiflorum L.)
1987. Jasnone, Êïs-
1989. Juniper (Berries) (Juniperus Communis L.)
1990. Juniper Oil (Juniperus Communis L.)
1991. Juniper, Extract (Juniperus Communis L.)
1992. Karaya, Gum (Sterculia Urens Roxb.)
1993. Kelp
1995. Labdanum, Absolute (Cistus Spp.)
1996. Labdanum, Oil (Cistus Spp.)
1997. Labdanum, Oleoresin (Cistus Spp.)
1998. Lactalbumin
1999. Lactalbumin Phosphate
2000. Lactase From Saccharomyces (Kluyveromyces) Lactis
2001. Lactase From Saccharomyces Fragilis
2002. Lactase Preparation, Candida Pseudotropicalis
2003. Lactic Acid
2004. Lactose
2005. Lactose, Hydrolyzed
2006. Lactylated Fatty Acid Esters Of Glycerol And Propylene Glycol
2007. Lactylic Esters Of Fatty Acids
2008. L-Alanine
2009. Lanolin
2010. L-Arabinose
2011. Lard
2012. Lard Oil
2013. L-Arginine
2014. L-Asparagine
2015. L-Aspartic Acid
2016. Laurel Berries (Laurus Nobilis L.)
2017. Lauric Acid
2018. Lauric Aldehyde
2019. Laurroyl Diethanolamide
2020. Lauryl Acetate
2021. Lauryl Alcohol
2022. Lavandin Absolute
2023. Lavandin, Concrete
2024. Lavandin, Oil
2025. Lavender (Lavandula Officinalis Chaix)
2026. Lavender, Absolute (Lavandula Officinalis Chaix)
2027. Lavender, Concrete (Lavandula Officinalis Chaix)
2028. Lavender, Oil (Lavandula Officinalis Chaix)
2029. Lavender, Spike (Lavandula Latifolia Bill.)
2030. Lavender, Spike, Oil (Lavandula Spp.)
2031. L-Carnitine
2032. L-Cysteine
2033. L-Cysteine Monohydrochloride
2034. L-Cystine
2035. Leche Caspi (Couma Macrocarpa Barb. Rodr.)
2036. Leche De Vaca (Brosimum Utile (H.B.K.) Pittier, And Poulsenia
2037. Lecithin
2038. Lecithin (Vegetable)
2039. Lecithin, Benzoyl Peroxide Modified
2040. Lecithin, Enzyme-Modified
2041. Lecithin, Hydrogen Peroxide Modified
2042. Leek Oil
2043. Lemon Essence
2044. Lemon Grass, Oil (Cymbopogon Citratus Dc. And Cymbopogon
2045. Lemon Peel Extract
2046. Lemon Peel Granules
2047. Lemon Terpenes
2048. Lemon Verbena, Oil (Lippia Citriodora)
2049. Lemon, Extract (Citrus Limon (L.) Burm. F.)
2050. Lemon, Juice
2051. Lemon, Oil (Citrus Limon (L.) Burm. F.)
2052. Lemon, Oil, Terpenesless (Citrus Limon (L.) Burm. F.)
2053. Lemon-Verbena (Lippia Citriodora Hbk.)
2054. Lepidine
2055. Levulinic Acid
2056. Levulose
2057. L-Glutamic Acid
2058. L-Glutamine
2059. L-Histidine
2060. L-Hydroxyproline
2061. Licorice (Glycyrrhiza Spp.)
2062. Licorice Extract (Glycyrrhiza Spp.)
2063. Licorice Extract Powder (Glycyrrhiza Spp.)
2064. Lignin
2065. Lignin Sodium Sulfonate
2066. Lignosulfonic Acid
2067. Lime Juice, Dehydrated
2068. Lime Oil, Distilled
2069. Lime Oil, Expressed
2070. Lime, Essence
2071. Lime, Juice
2072. Lime, Oil, Terpeneless (Citrus Aurantifolia (Christman) Swingle)
2073. Linaloe Wood, Oil (Bursera Delpechiana Poiss. And Other
2074. Linalool
2075. Linalool Oxide
2076. Linalyl Acetate
2077. Linalyl Anthranilate
2078. Linalyl Benzoate
2079. Linalyl Butyrate
2080. Linalyl Cinnamate
2081. Linalyl Formate
2082. Linalyl Hexanoate
2083. Linalyl Isobutyrate
2084. Linalyl Isovalerate
2085. Linalyl Octanoate
2086. Linalyl Phenylacetate
2087. Linalyl Propionate
2088. Linden Flowers (Tilia Glabra Vent.)
2089. Linden Flowers, Extract (Tilia Spp.)
2090. Linden Leaves (Tillia Spp.)
2091. Linoleic Acid
2092. Lipase
2093. Lipase From Animal Tissue
2094. Lipase From Aspergillus Niger
2095. Lipase From Aspergillus Oryzae
2096. Lipase From Rhizopus Niveus
2097. L-Isoleucine
2098. Litsea Cubeba Berry Oil
2099. L-Leucine
2100. L-Limonene
2101. L-Lysine
2102. L-Malic Acid
2103. L-Menthone 1,2-Glycerol Ketal
2104. L-Menthy 1,2-Propylene Glycol Carbonate
2105. L-Menthyl Ethylene Glycol Carbonate
2106. L-Menthyl Lactate
2107. L-Methionine
2108. Locust (Carob) Bean Gum
2109. Lovage (Levisticum Officinale Koch)
2110. Lovage, Extract (Levisticum Officinale Koch)
2111. Lovage, Oil (Levisticum Officinale Koch)
2112. L-Phenylalanine
2113. L-Proline
2114. L-Rhamnose
2115. L-Serine
2116. L-Threonine
2117. L-Tryptophan
2118. L-Tyrosine
2119. L-Tyrosine Ethyl Ester Hydrochloride
2120. Lungmoss (Sticta Pulmonacea Ach.)
2121. Lupulin (Humulus Lupulus L.)
2122. L-Valine
2123. Mace (Myristica Fragrans Houtt.)
2124. Mace, Oil (Myristica Fragrans Houtt.)
2125. Mace, Oleoresin (Myristica Fragrans Houtt.)
2126. Magnesium Caprate
2127. Magnesium Caprylate
2128. Magnesium Carbonate
2129. Magnesium Chloride
2130. Magnesium Cyclamate--Prohibited
2131. Magnesium Fumarate
2132. Magnesium Gluconate
2133. Magnesium Glycerophosphate
2134. Magnesium Hydroxide
2135. Magnesium Laurate
2136. Magnesium Myristate
2137. Magnesium Oleate
2138. Magnesium Oxide
2139. Magnesium Palmitate
2140. Magnesium Phosphate, Dibasic
2141. Magnesium Phosphate, Tribasic
2142. Magnesium Salts Of Fatty Acids
2143. Magnesium Silicate
2144. Magnesium Stearate
2145. Magnesium Sulfate
2146. Maidenhair Fern (Adiantum Capillus-Veneris L.)
2147. Malic Acid
2148. Malt
2149. Malt Syrup (Malt Extract)
2150. Maltodextrin
2151. Maltol
2152. Maltol Propionate
2153. Maltose
2154. Maltyl Isobutyrate
2155. Mandarin, Oil (Citrus Reticulata Blanco)
2156. Manganese Chloride
2157. Manganese Citrate
2158. Manganese Gluconate
2159. Manganese Glycerophosphate
2160. Manganese Hypophosphite
2161. Manganese Sulfate
2162. Manganous Oxide
2163. Mannitol
2164. Marigold, Pot (Calendula Officinalis L.)
2165. Marjoram Seed (Majorana Hortensis Moench (Origanum Majorana L.))
2166. Marjoram, Oleoresin (Majorana Hortensis Moench (Origanum
2167. Marjoram, Pot (Majorana Onites (L.) Benth. (Origanum Vulgare L.))
2168. Marjoram, Sweet (Majorana Hortensis Moench (Origanum Majorana L.))
2169. Marjoram, Sweet, Oil (Majorana Hortensis Moench (Origanum
2170. Massaranduba Balata (Manilkara Huberi (Ducke) Chevalier)
2171. Massaranduba Balata, Solvent-Free Resin Extract
2172. Massaranduba Chocolate (Manilkara Solimoesensis Gilly)
2173. Massoia Bark Oil
2174. Mastic Gum
2175. Mate, Absolute (Ilex Paraguariensis St. Hil.)
2176. Mate, Leaves
2177. M-Cresol
2178. M-Dimethoxybenzene
2179. Menadione Sodium Diphosphate
2180. Menhaden Oil
2181. Menhaden Oil, Hydrogenated
2182. Menhaden Oil, Partially Hydrogenated
2183. Menthadienol
2184. Menthol
2185. Menthone
2186. Menthone 1,2-Glycerol Ketal
2187. Menthone-8-Thioacetate
2188. Menthyl Acetate
2189. Menthyl Isovalerate
2190. Menthyl Propylene Glycol Carbonate
2191. Mesquite Wood Extract
2192. Methacrylic Acid-Divinylbenzene Copolymer
2193. Methoxyprazine
2194. Methyl (Methylthio)Acetate
2195. Methyl (Methylthio)Methyl Disulfide
2196. Methyl 1-Acetoxy-cyclohexyl Ketone
2197. Methyl 2-Decenoate
2198. Methyl 2-Furoate
2199. Methyl 2-Hexenoate
2200. Methyl 2-Hydroxy-4-Methylpentanoate
2201. Methyl 2-Methyl-3-Furyl Disulfide
2202. Methyl 2-Methylbutyrate
2203. Methyl 2-Methylpentanoate
2204. Methyl 2-Methylthiobutyrate
2205. Methyl 2-Nonenonoate
2206. Methyl 2-Nonynoate
2207. Methyl 2-Octenoate
2208. Methyl 2-Octynoate
2209. Methyl 2-Oxo-3-Methylpentanoate
2210. Methyl 2-Pyrrolyl Ketone
2211. Methyl 2-Thiofuroate
2212. Methyl 2-Undecynoate
2213. Methyl 3,7-Dimethyl-6-Octenoate
2214. Methyl 3-Hexenoate
2215. Methyl 3-Hydroxyhexanoate
2216. Methyl 3-Methyl-1-Butenyl Disulfide
2217. Methyl 3-Methylthiopropionate
2218. Methyl 3-Nonenonoate
2219. Methyl 3-Phenylpropionate
2220. Methyl 4-(Methylthio)Butyrate
2221. Methyl 4-Methylvalerate
2222. Methyl 4-Phenylbutyrate
2223. Methyl 9-Undecynoate
2224. Methyl Acetate
2225. Methyl Acrylate
2226. Methyl Acrylate-Divinylbenzene, Completely Hydrolyzed, Copolymer
2227. Methyl Acrylate-Dvb(2%), Copolymer, Aminolyzed With Dmapa
2228. Methyl Acrylate-Dvb(3.5%), Copolymer, Aminolyzed With Dmapa
2229. Methyl Acrylate–Dvb(–Deg-Divinyl Ether), Aminolyzed And
2230. Methyl Acrylate-Dvb-(Deg-Divinyl Ether), Aminolyzed, Terpolymer
2231. Methyl Acrylate-Dvb-Acrylonitrile, Completely Hydrolyzed, Terpolymer
2232. Methyl Alcohol
2233. Methyl Anisate
2234. Methyl Anthranilate
2235. Methyl Benzoeate
2236. Methyl Benzyl Disulfide
2237. Methyl Beta-Napthyl Ketone
2238. Methyl Butyrate
2239. Methyl Cinnamate
2240. Methyl Cis-4-Octenoate
2241. Methyl Cyclohexane-carboxylate
2242. Methyl Dihydrojasmonate
2243. Methyl Disulfide
2244. Methyl Esters Of Fatty Acids (Edible)
2245. Methyl Ethyl Sulfide
2246. Methyl Ethyl Trisulfide
2247. Methyl Furfuracrylate
2248. Methyl Furfuryl Disulfide
2249. Methyl Glucoside-Coconut Oil Ester
2250. Methyl Heptanoate
2251. Methyl Hexanoate
2252. Methyl Isobutyl Ketone
2253. Methyl Isobutyrate
2254. Methyl Isovalerate
2255. Methyl Jasmonate
2256. Methyl Laurate
2257. Methyl Linoleate (48%) Methyl Linolenate (52%) Mixture
2258. Methyl Mercaptan
2259. Methyl Methacrylate
2260. Methyl Myristate
2261. Methyl Nicotinate
2262. Methyl N-Methylanthranilate
2263. Methyl Nonanoate
2264. Methyl Octanoate
2265. Methyl O-Methoxybenzoate
2266. Methyl Phenethyl Ether
2267. Methyl Phenyl Disulfide
2268. Methyl Phenyl Sulfide
2269. Methyl Phenylacetate
2270. Methyl P-Hydroxybenzoate
2271. Methyl Propenyl Disulfide
2272. Methyl Propionate
2273. Methyl Propyl Disulfide
2274. Methyl Propyl Trisulfide
2275. Methyl P-Tert-Butylphenylacetate
2276. Methyl Salicylate
2277. Methyl Sorbate
2278. Methyl Sulfide
2279. Methyl Thiobutyrate
2280. Methyl Trans-2-Octenoate
2281. Methyl Valerate
2282. Methyl(E)-2-(Z)-4-Decadienoate
2283. Methyl-Alpha-Ionone
2284. Methylated Silica
2285. Methylbenzyl Acetate (Mixed O-, M-, P-)
2286. Methyl-Beta-Ionone
2287. Methylcyclopentenolone
2288. Methyl-Delta-Ionone
2289. Methylene Chloride
2290. Methylpolysilicone
2291. Methythio 2-(Acetyloxy)Propionate
2292. Methythio 2-(Propionyloxy)Propionate
2293. Methylthiomethyl Butyrate
2294. Methylthiomethyl Hexanoate
2295. Michelia Alba, Extract
2296. Microparticulated Protein Product
2297. Milk Clotting Enzyme From Bacillus Cereus (Frankland And Frankland)
2298. Milk Clotting Enzyme From Endothia Parasitica
2299. Milk Clotting Enzyme From Mucor Miehei Cooney Et Emerson
2300. Milk Clotting Enzyme From Mucor Pusillus L.
2301. Milk Clotting Enzyme, Aspergillus Oryzae Recombinant
2302. Milk Powder, Whole, Enzyme-Modified
2303. Mimosa Concrete (Acacia Decurrens Willd. Var. Dealbata)
2304. Mimosa, Absolute (Acacia Decurrens Willd. Var. Dealbata)
2305. Mineral Oil, White
2306. Mintlactone
2307. Molasses (Saccharum Officinarum L.)
2308. Molasses, Concentrate
2309. Molasses, Extract (Saccharum Officinarum L.)
2310. Molecular Sieve Resins
2311. Mono- And Diglycerides
2312. Mono- And Diglycerides, Acetic Acid Esters And Sodium And Calcium
2313. Mono- And Diglycerides, Acetyltartaric Acid Esters And
2314. Mono- And Diglycerides, Citric Acid Esters And Sodium And Calcium
2315. Mono- And Diglycerides, Diacetyltartaric Acid Esters
2316. Mono- And Diglycerides, Ethoxylated
2317. Mono- And Diglycerides, Lactic Acid Esters And Sodium And Calcium
2318. Mono- And Diglycerides, Monosodium Phosphate Derivatives
2319. Mono- And Diglycerides, Sodium Sulfoacetate Derivatives
2320. Monoammonium Glutamate
2321. Monochloracetic Acid—Prohibited
2322. Monoethanolamine
2323. Monoglyceride Citrate
2324. Monoglycerides, Acetylated
2325. Monoisopropyl Citrate
2326. Monomethyl Glutarate, L-
2327. Monomethyl Succinate
2328. Monopotassium Glutamate
2329. Monosodium Glutamate
2330. Montan Wax Fatty Acids, Oxidatively Refined, Polyhydric Alcohol Diesters
2331. Morpholine
2332. Morphinol, Fatty Acid Salts
2333. Mountain Maple (Acer Spicatum Lam.)
2334. Mountain Maple Bark (Acer Spicatum Lam.)
2335. Mountain Maple, Extract Solid (Acer Spicatum Lam.)
2336. Mullein Flowers (Verbascum Spp.)
2337. Musk Ambrette
2338. Musk Tonquin (Moschus Moschiferus L.)
2339. Musk, Ketone
2340. Mustard Flour
2341. Mustard Oil
2342. Mustard, Brown (Brassica Spp.)
2343. Mustard, Brown, Extract (Brassica Spp.)
2344. Mustard, Oriental
2345. Mustard, Yellow (Brassica Spp.)
2346. Mustard, Yellow, Extract (Brassica Spp.)
2347. Myristaldehyde
2348. Myristic Acid
2349. Myristyl Alcohol
2350. Myrrh, Extract
2351. Myrrh, Gum (Commiphora Spp.)
2352. Myrrh, Oil (Commiphora Spp.)
2353. Myrtenol
2354. Myrtenyl Acetate
2355. Myrtle Leaves (Myrtus Communis L.)
2356. Myrtle, Oil (Myrtus Communis L.)
2357. N-(4-Hydroxy-3-Methoxybenzyl)-8-Methyl-6-Nonenamide
2358. N-Acetyl-L-Methionine
2359. N-Alkyl(C8-C18 From Coconut Oil) Amine Acetate
2360. Naphtha
2361. Naringin, Extract (Citrus Paradisi Macf.)
2362. Natamycin
2363. Natural Gas
2364. N-Butane
2365. N-Butyl 2-Methylbutyrate
2366. Neohesperidin Dihydrochalcone
2367. Neotame
2368. Nerol
2369. Neroli, Bigarade Oil (Citrus Aurantium L.)
2370. Nerolidol
2371. Neryl Acetate
2372. Neryl Butyrate
2373. Neryl Formate
2374. Neryl Isobutyrate
2375. Neryl Isovalerate
2376. Neryl Propionate
2377. N-Ethyl-2-Isopropyl-5-Methylcyclohexane Carboxamide
2378. N-Furfurylpyrrole
2379. N-Hexyl 2-Butenoate
2380. Niacin
2381. Niacinamide
2382. Nickel
2383. Nicotinamide-Ascorbic Acid Complex
2384. Niger Gutta (Ficus Platypylla Del.)
2385. Nisin Preparation
2386. Nispero
2387. Nitrates, Sodium & Potassium
2388. Nitrites, Sodium & Potassium
2389. Nitrogen
2390. Nitrogen Oxides
2391. Nitrosyl Chloride
2392. Nitrous Oxide
2393. Nonanal
2394. Nonanoic Acid
2395. Nonanoyl 4-Hydroxy-3-Methoxybenzylamide
2396. Nonyl Acetate
2397. Nonyl Alcohol
2398. Nonyl Isovalerate
2399. Nonyl Octanoate
2400. Nootkatone
2401. Nordihydroguaiaretic Acid—Prohibited
2402. N-Undecylenzenesulfonic Acid
2403. Nutmeg (Myristica Fragrans Houtt.)
2404. Nutmeg Oleoresin
2405. Nutmeg, Oil (Myristica Fragrans Houtt.)
2406. O-(Ethoxymethyl)Phenol
2407. O-(Methylthio)Phenol
2408. Oak Chips, White, Extract (Quercus Alba L.)
2409. Oak Moss, Absolute (Euvemia Spp.)
2410. Oak Moss, Concrete (Euvemia Prunasti Spp.)
2411. Oak Wood, English (Quercus Robur L.)
2412. Oat Gum
2413. Ocimene
2414. O-Cresol
2415. Octadecylamine
2416. Octafluorocyclobutane
2417. Octahydrocoumarin
2418. Octanal
2419. Octanal Dimethyl Acetal
2420. Octanoic Acid
2421. Octyl 2-Furoate
2422. Octyl 2-Methylbutyrate
2423. Octyl Acetate
2424. Octyl Alcohol, Synthetic
2425. Octyl Butyrate
2426. Octyl Formate
2427. Octyl Gallate
2428. Octyl Heptanoate
2429. Octyl Isobutyrate
2430. Octyl Isovalerate
2431. Octyl Octanoate
2432. Octyl Phenylacetate
2433. Octyl Propionate
2434. Oiticica Oil
2435. Oleic Acid
2436. Oleic Acid, From Tall Oil Fatty Acids
2437. Olestra
2438. Olibanum, Absolute (Boswellia Spp.)
2439. Olibanum, Gum, Resin (Boswellia Spp.)
2440. Olibanum, Oil (Boswellia Spp.)
2441. Olibanum, Resinoid (Boswellia Spp.)
2442. Omega-6-Hexadecenlactone
2443. Omega-Pentadecalactone
2444. O-Methoxybenzaldehyde
2445. O-Methoxycinnamaldehyde
2446. O-Methylanisole
2447. Onion, Oil (Allium Cepa L.)
2448. Opopanax Tincture
2449. Opopanax, Gum
2450. Opopanax, Non-Specific
2451. Opopanax, Oil
2452. O-Propylphenol
2453. Orange B
2454. Orange Essence Oil, Natural
2455. Orange Essence, Natural
2456. Orange Flowers, Absolute (Citrus Aurantium L.)
2457. Orange Flowers, Bitter (Citrus Aurantium L)
2458. Orange Leaf, Absolute (Citrus Aurantium L.)
2459. Orange Peel
2460. Orange Peel, Bitter, Extract (Citrus Aurantium L.)
2461. Orange Peel, Bitter, Oil (Citrus Aurantium L.)
2462. Orange Peel, Sweet, Extract (Citrus Sinensis (L.) Osbeck)
2463. Orange Peel, Sweet, Oil (Citrus Sinensis (L.) Osbeck)
2464. Orange Peel, Sweet, Oil, Terpeneless (Citrus Sinensis (L.)
2465. Orange, Extract
2466. Orange, Juice
2467. Orange, Oil, Distilled (Citrus Sinensis (L.) Osbeck)
2468. Orange, Oil, Terpeneless (Citrus Sinensis (L.) Osbeck)
2469. Oregano (Lippia Spp., Usually L. Graveolens Hbk)
2470. Oregano (Other Genera Including Coleus, Lantana And Hptis)
2471. Oregano, European (Oiganum Spp.)
2472. Origanum Oil (Extractive)(Thymus Capitatus Hoff. Et Link)
2473. Orris Root, Extract (Iris Florentina L.)
2474. Orris, Concrete, Liquid, Oil (Iris Florentina L.)
2475. Osmanthus Absolute
2476. O-Toluenethiol
2477. O-Tolyl Acetate
2478. O-Tolyl Isobutyrate
2479. O-Tolyl Salicylalate
2480. O-Vinylanisole
2481. Ox Bile Extract
2482. Oxirane (Chloromethyl)-, Polymer With Ammonia, Reaction Product
2483. Oxystearin
2484. Ozone
2485. P,Alpha,Alpha-Trimethylbenzyl Alcohol
2486. P,Alpha-Dimethylbenzyl Alcohol
2487. P,Alpha-Dimethylstyrene
2488. P-4000--Prohibited
2489. Palmitic Acid
2490. P-Aminobenzoic Acid
2491. Pancreatin
2492. Pansy (Viola Tricolor L.)
2493. Papain (Carica Papaya L.)
2494. Paprika (Capsicum Annuum L.)
2495. Paprika Oleoresin (Capsicum Annuum L.)
2496. Paraffin And Succinic Derivatives, Synthetic
2497. Paraffin Wax
2498. Paraldehyde
2499. Parmesan Cheese, Reggiano Cheese
2500. Parsley (Petroselinum Spp.)
2501. Parsley, Oil (Petroselinum Spp.)
2502. Parsley, Oleoresin (Petroselinum Spp.)
2503. Passion Flower (Passiflora Incarnata L.)
2504. Passion Flower Extract
2505. Patchouly, Oil (Pogostemon Spp.)
2506. P-Cresol
2507. P-Cymene
2508. P-Dimethoxybenzene
2509. Peach Kernel, Extract (Prunus Persica Sieb Et Zucc.)
2510. Peach Leaves (Prunus Persica (L.) Batsch)
2511. Peach Leaves, Extract (Prunus Persica (L.) Batsch)
2512. Peanut Oil
2513. Peanut Stearine (Arachis Hypogaea L.)
2514. Pectin
2515. Pectin, Amidated
2516. Pectin, Modified
2517. Pectinase From Aspergillus Niger
2518. Pectinase From Bacillus Subtilis
2519. Pendare (Couma Macrocarpa Barb. Rodr. & Couma Utilis (Mart.)
2520. Penicillinase From Bacillus Subtilis
2521. Penicillium Roqueforti
2522. Pennyroyal, Oil, American (Hedeoma Pulegiodes (L.))
2523. Pennyroyal, Oil, European (Mentha Pulegium L.)
2524. Pentyl 2-Furyl Ketone
2525. Pepper, Black (Piper Nigrum L.)
2526. Pepper, Black, Oil (Piper Nigrum L.)
2527. Pepper, Black, Oleoresin (Piper Nigrum L.)
2528. Pepper, Cayenne
2529. Pepper, Red
2530. Pepper, White (Piper Nigrum L.)
2531. Pepper, White, Oil (Piper Nigrum L.)
2532. Pepper, White, Oleoresin (Piper Nigrum L.)
2533. Peppermint Leaves (Mentha Piperita L.)
2534. Peppermint Plant
2535. Peppermint, Oil (Mentha Piperita L.)
2536. Pepsin
2537. Peptones
2538. Peracetic Acid
2539. Perilla Leaf Oil
2540. Perillaldehyde
2541. Perillo
2542. Perillyl Acetate
2543. Periodic Acid
2544. P-Ethoxybenzaldehyde
2545. P-Ethylphenol
2546. Petitgrain, Lemon, Oil (Citrus Limon (L.) Burm. F.)
2547. Petitgrain, Mandarin, Oil (Citrus Reticulata Blanco Var. Mandarin)
2548. Petitgrain, Oil (Citrus Aurantium L.)
2549. Petrolatum
2550. Petroleum Hydrocarbons, Odorless, Light
2551. Petroleum Naphtha
2552. Petroleum Wax
2553. Petroleum Wax, Synthetic
2554. Phaffia Yeast
2555. Phenethyl 2-Furoate
2556. Phenethyl 2-Methylbutyrate
2557. Phenethyl Acetate
2558. Phenethyl Alcohol
2559. Phenethyl Anthranilate
2560. Phenethyl Benzoate
2561. Phenethyl Butyrate
2562. Phenethyl Cinnamate
2563. Phenethyl Formate
2564. Phenethyl Hexanoate
2565. Phenethyl Isobutyrate
2566. Phenethyl Isothiocyanate
2567. Phenethyl Isovalerate
2568. Phenethyl Octanoate
2569. Phenethyl Phenylacetate
2570. Phenethyl Propionate
2571. Phenethyl Salicylate
2572. Phenethyl Sencioate
2573. Phenethyl Tigliate
2574. Phenethylamine
2575. Phenol
2576. Phenoil-Formaldehyde, Cross-Linked, Tetraethylenepentamine Activated
2577. Phenoil-Formaldehyde, Cross-Linked, Triethylenetetramine &
2578. Phenoil-Formaldehyde, Cross-Linked, Triethylenetetramine Activated
2579. Phenoil-Formaldehyde, Sulfite-Modified, Cross-Linked
2580. Phenoxyacetic Acid
2581. Phenyl Acetate
2582. Phenyl Disulfide
2583. Phenylacetaldehyde
2584. Phenylacetaldehyde 2,3-Butylene Glycol Acetal
2585. Phenylacetaldehyde Diisobutyl Acetal
2586. Phenylacetaldehyde Dimethyl Acetal
2587. Phenylacetaldehyde Glyceryl Acetal
2588. Phenylacetic Acid
2589. Phenylethyl Mercaptan
2590. Phosphoric Acid
2591. Phosphorus Oxichloride
2592. Pimenta Leaf, Oil (Pimenta Officinalis Lindl.)
2593. Pine Bark, White (Pinus Strobus L.)
2594. Pine Bark, White, Extract Solid (Pinus Strobus L.)
2595. Pine Bark, White, Oil (Pinus Strobus L.)
2596. Pine Needle, Dwarf, Oil (Pinus Mugo Turra Var. Pumilio (Haenke)
2597. Pine Tar, Oil (Pinus Spp.)
2598. Pine, Scotch, Oil (Pinus Sylvestris L.)
2599. Pine, White, Oil (Pinus Spp.)
2600. Pinocarveol
2601. Piperazine Dihydrochloride
2602. Piperidine
2603. Piperine
2604. Piperitenone
2605. Piperitenone Oxide
2606. Piperonal
2607. Piperonyl Acetate
2608. Piperonyl Isobutyrate
2609. Pipsissewa Leaves, Extract (Chimaphila Umbellata Nutt.)
2610. P-Isopropylacetonophene
2611. P-Isopropylbenzyl Alcohol
2612. P-Isopropylphenylacetalddehyde
2613. P-Menth-1-En-3-Ol
2614. P-Menth-1-Ene-9-Al
2615. P-Menth-3-En-1-OI
2616. P-Mentha-1,8-Dien-7-OI
2617. P-Mentha-8-Thiol-3-One
2618. P-Menthanc-2-One
2619. P-Methoxy-Alpha-Methylcinnamaldehyde
2620. P-Methoxybenzaldehyde
2621. P-Methoxycinnamaldehyde
2622. P-Methylanisole
2623. P-Methylcinnamaldehyde
2624. Poly(Acrylic Acid-Co-Hypophosphite), Sodium Salt
2625. Poly(Alkyl(C16-22)Acrylate)
2626. Poly(Divinylbenzene-Co-Ethylstyrere)
2627. Poly(Divinylbenzene-Co-Trimethyl(Vinylbenzyl)Ammonium Chloride)
2628. Poly(Maleic Anhydride), Sodium Salt
2629. Polyacrylamide
2630. Polyacrylamide Resin, Modified
2631. Polyacrylic Acid, Sodium Salt
2632. Polydextrose
2633. Polyethylene (M W 2,000-21,000)
2634. Polyethylene Glycol (400) Dioleate
2635. Polyethylene Glycol (M W 200-9,500)
2636. Polyethylene, Oxidized
2637. Polyethyleneimine Reaction Product W/ 1,2-Dichloroethane
2638. Polyglycerol Esters Of Fatty Acids
2639. Polyglyceryl Phthalate Ester Of Coconut Oil Fatty Acids
2640. Polysisobutylene (Min M W 37,000)
2641. Polylimonene
2642. Polymaleic Acid
2643. Polymaleic Acid, Sodium Salt
2644. Polyoxyethylene (600) Dioleate
2645. Polyoxyethylene (600) Mono- Ricinoleate
2646. Polyoxymethylene 40 Monostearate
2647. Polyoxymethylene Dioleate
2648. Polypropylene Glycol (M W 1,200-3,000)
2649. Polysorbate 20
2650. Polysorbate 60
2651. Polysorbate 65
2652. Polysorbate 80
2653. Polystyrene, Cross-Linked, Chloromethylated, Then Aminated
2654. Polyvinyl Acetate
2655. Polyvinyl Alcohol
2656. Polyvinyl Polypyrrolidone
2657. Polyvinylpyrrolidone
2658. Pomegranate Bark, Extract (Punica Granatum L.)
2659. Polpar Buds (Populus Spp.)
2660. Poppy Seed (Papaver Somniferum L.)
2661. Potassium 2-(1'-Ethoxy)Ethoxypropanoate
2662. Potassium Acetate
2663. Potassium Acid Pyrophosphate
2664. Potassium Acid Tartrate
2665. Potassium Benzoate
2666. Potassium Bicarbonate
2667. Potassium Bisulfite
2668. Potassium Borate
2669. Potassium Bromate
2670. Potassium Bromide
2671. Potassium Caprate
2672. Potassium Caprylate
2673. Potassium Carbonate
2674. Potassium Caseinate
2675. Potassium Chloride
2676. Potassium Citrate
2677. Potassium Cyclamate—Prohibited
2678. Potassium Fumarate
2679. Potassium Gibberellate
2680. Potassium Gluconate
2681. Potassium Glycerophosphate
2682. Potassium Hydroxide
2683. Potassium Hypophosphatate
2684. Potassium Hypophosphite
2685. Potassium Iodate
2686. Potassium Iodide
2687. Potassium Lactate
2688. Potassium Laurate
2689. Potassium Metabisulfite
2690. Potassium Myristate
2691. Potassium Nitrate
2692. Potassium Nitrite
2693. Potassium N-Methylthiocarbamate
2694. Potassium Oleate
2695. Potassium Palmitate
2696. Potassium Pectinate
2697. Potassium Permanganate
2698. Potassium Persulfate
2699. Potassium Phosphate, Monobasic
2700. Potassium Phosphate, Tribasic
2701. Potassium Polymetaphosphate
2702. Potassium Pyrophosphate
2703. Potassium Salts Of Fatty Acids
2704. Potassium Sorbate
2705. Potassium Stearate
2706. Potassium Sulfate
2707. Potassium Sulfite
2708. Potassium Tripolyphosphate
2709. Potato Starch
2710. P-Propylanisole
2711. P-Propylphenol
2712. Prenyl Thioacetate
2713. Prenylthiol
2714. Prickly Ash Bark Extract (Xanthoxylum Spp.)
2715. Prickly Ash Bark, Oil
2716. Propane
2717. Propenyl Propyl Disulfide
2718. Propenylguaethol
2719. Propionaldehyde
2720. Propionic Acid
2721. Propiophenone
2722. Propyl 2,4-Decadienoate
2723. Propyl 2-Furanacrylate
2724. Propyl 2-Furoate
2725. Propyl 2-Methyl-3-Furyl Disulfide
2726. Propyl Acetate
2727. Propyl Alcohol
2728. Propyl Benzoate
2729. Propyl Butyrate
2730. Propyl Cinnamate
2731. Propyl Disulfide
2732. Propyl Formate
2733. Propyl Gallate
2734. Propyl Heptanoate
2735. Propyl Hexanoate
2736. Propyl Isobutyrate
2737. Propyl Isovalerate
2738. Propyl Mercaptan
2739. Propyl Phenylacetate
2740. Propyl P-Hydroxybenzoate
2741. Propyl Propionate
2742. Propyl Thioacetate
2743. Propylene Chlorohydrin
2744. Propylene Glycol
2745. Propylene Glycol Alginate
2746. Propylene Glycol Dibenzoate
2747. Propylene Glycol Mono- And Diesters Of Fats And Fatty Acids
2748. Propylene Glycol Stearate
2749. Propylene Oxide
2750. Protease From Aspergillus Flavus
2751. Protease From Aspergillus Niger
2752. Protease From Aspergillus Oryzae
2753. Protease From Bacillus Amyloliquefaciens
2754. Protease From Bacillus Licheniformis
2755. Protease From Bacillus Subtilis
2756. Protein Hydrolysate, Unspecified
2757. Protein, Animal, Hydrolyzed
2758. Protein, Milk, Hydrolyzed
2759. Protein, Vegetable, Hydrolyzed
2760. Psyllium Seed Husk
2761. P-Tolyl 3-Methylbutyrate
2762. P-Tolyl Acetate
2763. P-Tolyl Isobutyrate
2764. P-Tolyl Laurate
2765. P-Tolyl Octanoate
2766. P-Tolyl Phenylacetate
2767. P-Tolylacetalddehyde
2768. Pulegone
2769. Pulp
2770. P-Vinylphenol
2771. Pyrazine
2772. Pyrazine Ethanethiol
2773. Pyrazinyl Methyl Sulfide
2774. Pyridine
2775. Pyridoxine
2776. Pyridoxine Hydrochloride
2777. Pyrroligneous Acid
2778. Pyrroligneous Acid, Extract
2779. Pyrrrole
2780. Pyrrolidine
2781. Pyruvaldehyde
2782. Pyruvic Acid
2783. Quassia, Extract (Picrasma Excelsa (Sw.) Planch Or Quassia Amara L.)
2784. Quaternary Ammonium Chloride Combination
2785. Quebracho Bark Extract
2786. Quillaja (Quillaja Saponaria Molina)
2787. Quillaja Extract (Quillaja Saponaria Molina)
2788. Quince Seed, Extract (Cydonia Spp.)
2789. Quinine Bisulfate
2790. Quinine Hydrochloride
2791. Quinine Sulfate
2792. Quinoline
2793. Rapeseed Oil, Hydrogenated
2794. Rapeseed Oil, Hydrogenated, Superglycerinated
2795. Rapeseed Oil, Low Erucic Acid
2796. Rapeseed Oil, Low Erucic Acid, Partially Hydrogenated
2797. Rennet
2798. Resin, From Formaldehyde, Acetone, And Tetraethylenepentamine
2799. Resorcinol
2800. Rhatany, Extract (Krameria Spp.)
2801. Rhodinol
2802. Rhodinyl Acetate
2803. Rhodinyl Butyrate
2804. Rhodinyl Formate
2805. Rhodinyl Isobutyrate
2806. Rhodinyl Isovalerate
2807. Rhodinyl Phenylacetate
2808. Rhodinyl Propionate
2809. Rhubarb Root (Rheum Spp.)
2810. Rhubarb, Garden Root (Rheum Rhamonticum L.)
2811. Riboflavin
2812. Riboflavin 5'-Phosphate
2813. Riboflavin 5'-Phosphate, Sodium
2814. Rice Bran Wax
2815. Rice Starch
2816. Rice, Milled
2817. Rose Flowers (Rosa Spp.)
2818. Rose Hips, Extract (Rosa Spp.)
2819. Rose Leaves (Rosa Spp.)
2820. Rose Water, Stronger (Rosa Centifolia L.)
2821. Rose, Absolute (Rosa Spp.)
2822. Rose, Bud (Rosa Spp.)
2823. Rose, Oil (Rosa Spp.)
2824. Roselle (Hibiscus Sabdariffa L.)
2825. Rosemary (Rosmarinus Officinalis L.)
2826. Rosemary, Extract (Rosmarinus Officinalis L.)
2827. Rosemary, Oil (Rosmarinus Officinalis L.)
2828. Rosemary, Oleoresin
2829. Rosidinha (Micropholis Also Known As Sideroxylon) Spp.
2830. Rosin (Pinus Spp.) And Rosin Derivatives
2831. Rosin, Adduct With Fumaric Acid, Pentaerythritol Ester
2832. Rosin, Gum Or Wood, Partially Hydrogenated, Glycerol Ester
2833. Rosin, Gum Or Wood, Partially Hydrogenated, Pentaerythritol Ester
2834. Rosin, Gum Or Wood, Pentaerythritol Ester
2835. Rosin, Gum, Glycerol Ester
2836. Rosin, Limed
2837. Rosin, Methyl Ester, Partially Hydrogenated
2838. Rosin, Partially Dimerized, Calcium Salt
2839. Rosin, Partially Dimerized, Glycerol Ester
2840. Rosin, Partially Hydrogenated
2841. Rosin, Polymerized, Glycerol Ester
2842. Rosin, Tall Oil, Glycerol Ester
2843. Rosin, Wood
2844. Rosin, Wood, Glycerol Ester
2846. Rosin, Wood, Maleic Anhyd. Mod., Pentaerythritol Ester, Acid #176-186
2847. Rubber, Natural-Smoked Sheet And Latex Solids (Hevea Brasiliensis)
2848. Rue (Ruta Graveolens L.)
2849. Rue, Oil (Ruta Graveolens L.)
2850. Rum
2851. Rum Ether
2852. Rutin
2853. S-(Tetrahydro-2,5-Dimethyl-3-Furanyl) Ethanethioate
2854. Saccharin
2855. Saccharin, Ammonium Salt
2856. Saccharin, Calcium Salt
2857. Saccharin, Sodium Salt
2858. Saffron (Crocus Sativus L.)
2859. Saffron, Extract (Crocus Sativus L.)
2860. Safrole-Free Extract Of Sassafras
2861. Safrole--Prohibited
2862. Sage (Salvia Officinalis L.)
2863. Sage, Greek (Salvia Triloba L.)
2864. Sage, Oil (Salvia Officinalis L.)
2865. Sage, Oleoresin (Salvia Officinalis L.)
2866. Sage, Spanish, Oil (Salvia Lavandulaefolia Vahl.)
2867. Salicylaldehyde
2868. Salicylic Acid
2869. Salts Of Fatty Acids
2870. Sandalwood, Red (Pterocarpus Santalinus L.F.)
2871. Sandalwood, White (Santalum Album L.)
2872. Sandalwood, Yellow, Oil (Santalum Album L.)
2873. Sandarac (Tetracrinis Articulata (Vahl.) Mast.)
2874. Santalol (Alpha And Beta)
2875. Santalol, Alpha
2876. Santalol, Beta
2877. Santalyl Acetate
2878. Santalyl Phenylacetate
2879. Sarcodactylis Oil
2880. Sarsaparilla, Extract (Smilax Spp.)
2881. Sassafras Bark, Extract (Safrole-Free) (Sassafras Albidum
2882. Sassafras Leaves (Safrole-Free) (Sassafras Albidum (Nutt.) Nees)
2883. Sausage Casings (Hcl And Cellulose Fibers)
2884. Savory, Summer (Satureja Hortensis L.)
2885. Savory, Summer, Oil (Satureja Hortensis L.)
2886. Savory, Summer, Oleoresin (Satureja Hortensis L.)
2887. Savory, Winter (Satureja Montana L.)
2888. Savory, Winter, Oil (Satureja Montana L.)
2889. Savory, Winter, Oleoresin (Satureja Montana L.)
2890. Schinus Molle, Oil (Schinus Molle L.)
2891. Sclareolide
2892. Sec-Butyl Ethyl Ether
2893. Senna, Alexandria (Cassia Acutifolia Delile)
2894. Serpentaria (Aristolochia Serpentaria L.)
2895. Sesame (Sesamum Indicum L.)
2896. Sheanut Oil
2897. Shellec Wax
2898. Shellec, Purified
2899. Silica Aerogel
2900. Silicon Dioxide
2901. Silver Fir, Needles And Twigs, Oil (Abies Alba Mill.)
2902. Silver-Silver Dragees
2903. Simaruba Bark (Simaruba Amara Aubl.)
2904. Skatole
2905. Sloe Berries (Prunus Spinosa L.)
2906. Sloe Berries, Extract (Prunus Spinosa L.)
2907. Sloe Berries, Extract Solid (Prunus Spinosa L.)
2908. S-Methyl 3-Methylbutanethioate
2909. S-Methyl 4-Methylpentanethioate
2910. S-Methyl Benzothioate
2911. S-Methyl Hexanethioate
2912. S-Methyl Thioacetate
2913. Snakeroot, Canadian, Oil (Asarum Canadense L.)
2914. Sodium (4-Methoxybenzoyloxy)Acetate
2915. Sodium 2-(4-Methoxyphenoxy)Propanoate
2916. Sodium 2-Ethylhexyl Sulfate
2917. Sodium 3-Mercaptooxopropionate
2918. Sodium 3-Methoxy-4-Hydroxycinnamate
2919. Sodium Acetate
2920. Sodium Acid Pyrophosphate
2921. Sodium Aluminate
2922. Sodium Aluminum Phosphate, Acidic Or Basic
2923. Sodium Aluminum Silicate
2924. Sodium Ascorbate
2925. Sodium Benzoate
2926. Sodium Bicarbonate
2927. Sodium Bisulfite
2928. Sodium Borate
2929. Sodium Borohydride
2930. Sodium Calcium Aluminosilicate, Hydrated
2931. Sodium Caprate
2932. Sodium Caprylate
2933. Sodium Carbonate
2934. Sodium Caseinate
2935. Sodium Chloride
2936. Sodium Chlorite
2937. Sodium Copper Chlorophyllin
2938. Sodium Cyclamate--Prohibited
2939. Sodium Decylbenzenesulfonate
2940. Sodium Dehydroacetate
2941. Sodium Diacetate
2942. Sodium Dimethyldithiocarbamate
2943. Sodium Dodecylbenzenesulfonate
2944. Sodium Erythorbate
2945. Sodium Ferricitropyrophosphate
2946. Sodium Ferritriopolyphosphate
2947. Sodium Fluoride
2948. Sodium Formate
2949. Sodium Fumarate
2950. Sodium Glucoheptonate
2951. Sodium Gluconate
2952. Sodium Hexametaphosphate
2953. Sodium Humate
2954. Sodium Hydrosulfite
2955. Sodium Hydroxide
2956. Sodium Hypochlorite
2957. Sodium Hypophosphite
2958. Sodium Lactate
2959. Sodium Laurate
2960. Sodium Lauryl Sulfate
2961. Sodium Metabisulfite
2962. Sodium Metaphosphate
2963. Sodium Metasilicate
2964. Sodium Methyl Sulfate
2965. Sodium Mono- And Dimethyl Naphthalene Sulfonates
2966. Sodium Myristate
2967. Sodium N-Alkylbenzenesulfonate
2968. Sodium Nitrate
2969. Sodium Nitrite
2970. Sodium Oleate
2971. Sodium Palmitate
2972. Sodium Pantothenate
2973. Sodium Pectinate
2974. Sodium Phosphate, Dibasic
2975. Sodium Phosphate, Monobasic
2976. Sodium Phosphate, Tribasic
2977. Sodium Polymethacrylate
2978. Sodium Potassium Tartrate
2979. Sodium Propionate
2980. Sodium Pyrophosphate
2981. Sodium Salts Of Fatty Acids
2982. Sodium Sesquicarbonate
2983. Sodium Silicate
2984. Sodium Sorbate
2985. Sodium Stearate
2986. Sodium Stearoyl-2-Lactylate
2987. Sodium Stearyl Fumarate
2988. Sodium Sulfate
2989. Sodium Sulfide
2990. Sodium Sulfites
2991. Sodium Tartrate
2992. Sodium Taurocholate
2993. Sodium Thiosulfate
2994. Sodium Triopolyphosphate
2995. Sodium Zinc Metasilicate
2996. Sorbic Acid
2997. Sorbitan Monooleate
2998. Sorbitan Monostearate
2999. Sorbose
3000. Soy Concentrate, Enzyme Activated
3001. Soy Protein, Isolate
3002. Soya Bean Oil Fatty Acids, Hydroxylated
3003. Soya Fatty Acid Amine, Ethoxylated
3004. Soybean Oil, Epoxidized
3005. Soybean Oil, Hydrogenated
3006. Spearmint (Mentha Spicata L.)
3007. Spearmint, Extract (Mentha Spicata L.)
3008. Spearmint, Oil (Mentha Spicata L.)
3009. Sperm Oil
3010. Sperm Oil, Hydrogenated
3011. Spikenard Extract
3012. Spiro(2,4-Dithia-1-Methyl-8-Oxabicyclo(3.3.0)Octane-3,3'-{1'-Oxa-2'-Me
3013. Spruce Needles And Twigs, Extract (Picea Spp.)
3014. Spruce Needles And Twigs, Oil (Picea Spp.)
3015. St. Johnswort Leaves, Flowers And Caulis (Hypericum Perforatum.)
3016. Stannic Chloride
3017. Stannous Chloride
3018. Starch, Acid Modified
3019. Starch, Alpha-Amylase Modified
3020. Starch, Bleached
3021. Starch, Food, Modified
3022. Starch, Food, Modified: Acetylated Distarch Adipate
3023. Starch, Food, Modified: Acetylated Distarch Glycerol
3024. Starch, Food, Modified: Acetylated Distarch Oxypropanol
3025. Starch, Food, Modified: Acetylated Distarch Phosphate
3026. Starch, Food, Modified: Beta-Amylase Modified Starch
3027. Starch, Food, Modified: Beta-Amylase Sodium Starch Octenylsuccinate
3028. Starch, Food, Modified: Distarch Glycerol
3029. Starch, Food, Modified: Distarch Oxypropanol
3030. Starch, Food, Modified: Distarch Phosphate (From Phosphorus
Oxychloride)
3031. Starch, Food, Modified: Distarch Phosphate (From Sodium
Trimethylphosphate)
3032. Starch, Food, Modified: Hydroxypropyl Distarch Glycerol
3033. Starch, Food, Modified: Hydroxypropyl Distarch Phosphate
3034. Starch, Food, Modified: Hydroxypropyl Starch
3035. Starch, Food, Modified: Isoamylase Modified Starch
3036. Starch, Food, Modified: Oxidized Hydroxypropyl Starch
3037. Starch, Food, Modified: Oxidized Starches
3038. Starch, Food, Modified: Phosphated Distarch Phosphate
3039. Starch, Food, Modified: Pullulanase Modified Starch
3040. Starch, Food, Modified: Starch Acetate
3041. Starch, Food, Modified: Starch Aluminum Octenyl Succinate
3042. Starch, Food, Modified: Starch Phosphate
3043. Starch, Food, Modified: Starch Sodium Octenyl Succinate
3044. Starch, Food, Modified: Starch Sodium Succinate
3045. Starch, Food, Modified: Succinyl Distarch Glycerol
3046. Starch, Food, Modified: Glucoamylase Modified Starch
3047. Starch, Pregelatinized
3048. Starch, Unmodified
3049. Stearic Acid
3050. Stearyl Alcohol
3051. Stearyl Alcohol, Plus Beeswax
3052. Stearyl Citrate
3053. Stearyl Monoglyceridyl Citrate
3054. Storax (Liquidambar Spp.)
3055. Storax Extract (Liquidambar Spp.)
3056. Storax Oil
3057. Styrene
3058. Styrene, Divinylbenzene, Sulfonated Copolymer
3059. Styrene-Divinylbenzene Copolymer, Chloromethylated, Aminated, Oxidized
3060. Styrene-Divinylbenzene-Acrylonitrile, Sulfonated Terpolymer
3061. Styrene-Divinylbenzene-Methyl Acrylate, Sulfonated Terpolymer
3062. Styrene-Dvb-Acrylonitrile-Methyl Acrylate, Sulfonated Tetrapolymer
3063. Succinic Acid
3064. Succinic Anhydride
3065. Succinylated Gelatin
3066. Succinylated Monoglycerides
3067. Succistearin
3068. Sucralose
3069. Sucrose
3070. Sucrose Acetate Isobutyrate
3071. Sucrose Fatty Acid Esters
3072. Sucrose Liquid
3073. Sucrose Octaacetate
3074. Sugar Beet Extract Flavor Base
3075. Sulfamic Acid
3076. Sulfites, Strong Alkali
3077. Sulfiting Agents
3078. Sulfopropyl Cellulose
3079. Sulfur Dioxide
3080. Sulfuric Acid
3081. Sulphurous Acid
3082. Tagetes Meal & Extract
3083. Tagetes, Oil (Tagetes Spp.)
3084. Talc
3085. Tall Oil
3086. Tallow Alcohol, Hydrogenated
3087. Tallow Flakes
3088. Tallow, Beef
3089. Tallow, Hydrogenated
3090. Tallow, Hydrogenated, Oxidized Or Sulfated
3091. Tamarind Extract (Tamarindus Indica L.)
3092. Tamarinds
3093. Tangerine, Essence
3094. Tangerine, Extract (Citrus Reticulata Blanco)
3095. Tangerine, Oil (Citrus Reticulata Blanco)
3096. Tannic Acid
3097. Tansy (Tanacetum Vulgara L.)
3098. Tansy, Oil (Tanacetum Vulgara L.)
3099. Tapioca Starch
3100. Tarragon (Artemisia Dracunculus L.)
3101. Tarragon Extract (Artemisia Dracunculus L.)
3102. Tarragon Oil (Artemisia Dracunculus L.)
3103. Tartaric Acid, L
3104. Taurine
3105. Taurocholic Acid
3106. Tea Extract (Thea Sinensis L.)
3107. Tea Tree Oil (Melaleuca Alternifolia)
3108. Terpene Resin
3109. Terpene Resins, Natural
3110. Terpene Resins, Synthetic
3111. Terpinolene
3112. Terpinyl Acetate
3113. Terpinyl Butyrate
3114. Terpinyl Cinnamate
3115. Terpinyl Formate
3116. Terpinyl Isobutyrate
3117. Terpinyl Isovalerate
3118. Terpinyl Propionate
3119. Tert-Butylhydroquinone
3120. Tetraethylenepentamine Crosslinked With Epichlorohydrin
3121. Tetrahydro-4-Methyl-2-(2-Methylpropen-1-Yl)Pyran
3122. Tetrahydrofurfuryl Acetate
3123. Tetrahydrofurfuryl Alcohol
3124. Tetrahydrofurfuryl Butyrate
3125. Tetrahydrofurfuryl Cinnamate
3126. Tetrahydrofurfuryl Propionate
3127. Tetrahydroinalool
3128. Tetrahydro-Pseudo-Ionone
3129. Tetramethyl Ethylcyclohexenone (Mixture Of Isomers)
3130. Thaumatin
3131. Thaumatin B, Recombinant
3132. Theaspirane
3133. Theobromine
3134. Thiamine
3135. Thiamine Hydrochloride
3136. Thiamine Mononitrate
3137. Thiazole
3138. Thiodipropionic Acid
3139. Thiogeraniol
3140. Thiourea--Prohibited
3141. Thistle, Blessed (Cnicus Benedictus L.)
3142. Thistle, Blessed, Extract (Cnicus Benedictus L.)
3143. Thistle, Blessed, Extract Solid (Cnicus Benedictus L.)
3144. Thistle, Blessed, Oil (Cnicus Benedictus L.)
3145. Thyme (Thymus Serpyllum L.)
3146. Thyme (Thymus Vulgaris L.)
3147. Thyme Oil (Thymus Vulgaris L. And T. Zygis Var. Gracilis Boiss.)
3148. Thyme Oleoresin
3149. Thyme, Extract
3150. Thyme, Wild Or Creeping, Extract (Thymus Serpyllum L.)
3151. Thymol
3152. Titanium Dioxide
3153. Tocopherols
3154. Tolu, Balsam, Extract (Myroxylon Spp.)
3155. Tolu, Balsam, Gum (Myroxylon Spp.)
3156. Tolu aldehyde Glyceryl Acetal (Mixed O-, M-, P-)
3157. Tolu aldehydes (Mixed O-, M-, P-)
3158. Tragacanth, Gum (Astragalus Spp.)
3159. Trans, Trans-2,4-Hexadienial
3160. Trans,Trans-2,4-Dodecadienial
3161. Trans,Trans-2,4-Octadienial
3162. Trans-2-Hexen-1-Yl Acetate
3163. Trans-2-Hexenoic Acid
3164. Trans-2-Methyl-2-Butenoic Acid
3165. Trans-2-Nonen-1-OI
3166. Trans-2-Octen-1-Yl Acetate
3167. Trans-2-Octen-1-Yl Butanoate
3168. Trans-3-Heptenyl 2-Methylpropanoate
3169. Trans-3-Heptenyl Acetate
3170. Trans-3-Hexenal
3171. Trans-3-Octen-2-OI
3172. Trans-Anethole
3173. Trefoil, Sweet (Melilotus Coerulea)
3174. Triacetin (Glycerol Triacetate)
3175. Tributyl Acetylcitrate
3176. Trichloroethylene
3177. Tridodecyl Amine
3178. Triethanolamine
3179. Triethyl Citrate
3180. Triethylenetetramine Cross-Linked With Epichlorohydrin
3181. Trifluoromethane Sulfonic Acid
3182. Trimethylamine
3183. Trisodium Citrate
3184. Trisodium Nitrotriacetate
3185. Trithioacetone
3186. Trypsin From Animal Tissue
3187. Tuberose, Oil (Polianthes Tuberosa L.)
3188. Tunu (Castilla Fallax Cook)
3189. Turmeric (Curcuma Longa L.)
3190. Turmeric, Extract (Curcuma Longa L.)
3191. Turmeric, Oleoresin (Curcuma Longa L.)
3192. Turpentine, Gum (Pinus Spp.)
3193. Turpentine, Rectified
3194. Turpentine, Steam Distilled (Pinus Spp.)
3195. Ultramarine Blue
3196. Undecanal
3197. Undecanoic Acid
3198. Undecen-1-OI
3199. Undecyl Alcohol
3200. Urea
3201. Urease Enzyme Preparation (Lactobacillus Fermentum)
3202. Valencene
3203. Valeraldehyde
3204. Valerian Root, Extract (Valeriana Officinalis L.)
3205. Valerian Root, Oil (Valeriana Officinalis L.)
3206. Valeric Acid
3207. Vanilla (Vanilla Spp.)
3208. Vanilla, Absolute (Vanilla Spp.)
3209. Vanilla, Extract (Vanilla Spp.)
3210. Vanilla, Oleoresin (Vanilla Spp.)
3211. Vanillic Acid
3212. Vanillin
3213. Vanillin 1,2-Butylene Glycol Acetal
3214. Vanillin 3-(L-Menthoxy)Propane-1,2-Diol
3215. Vanillin Acetate
3216. Vanillin Isobutyrate
3217. Vanillin Propylene Glycol Acetal
3218. Vanillyl Alcohol
3219. Vanillyl Butyl Ether
3220. Vanillyl Ethyl Ether
3221. Vanillylidene Acetone
3222. Vegetable Gums, Other Than Those Cfr Listed
3223. Vegetable Juice
3224. Veratraldehyde
3225. Verbenol
3226. Veronica (Veronica Officinalis L.)
3227. Vervain, European (Verbena Officinalis L.)
3228. Vetiver (Vetiveria Zizaniodes Stapf)
3229. Vetiver, Oil (Vetiveria Zizanioides Stapf)
3230. Vetiveryl Acetate
3231. Vinyl Acetate
3232. Vinyl Chloride-Vinylidene Chloride Copolymer
3233. Violet Leaves Absolute (Viola Odorata L.)
3234. Violet, Swiss (Viola Calcarata L.)
3235. Vitamin A
3236. Vitamin A Acetate
3237. Vitamin A Palmitate
3238. Vitamin B Complex And Syrup
3239. Vitamin B-12
3240. Vitamin D
3241. Vitamin D-2
3242. Vitamin D-3
3243. Vitamin K
3244. Walnut Hull, Extract (Juglans Spp.)
3245. Walnut Leaves, Extract (Juglans Spp.)
3246. Wheat Gluten
3247. Wheat Starch
3248. Whey
3249. Whey Protein Concentrate
3250. Whey, Delactosed
3251. Whey, Demineralized
3252. Whey, Partially Dimineralized And Partially Delactosed
3253. Wintergreen, Extract (Gaultheria Procumbens L.)
3254. Wintergreen, Oil (Gaultheria Procumbens L.)
3255. Woodruff, Sweet (Asperula Odorata L.)
3256. Wort
3257. Xanthan Gum
3258. Xanthophyll
3259. Xyitol
3260. Yarrow, Herb (Achillea Millefolium L.)
3261. Yarrow, Oil (Achillea Millefolium L.)
3262. Yeast Autolysate
3263. Yeast Extract Autolyzed
3264. Yeast, Dried Irradiated
3265. Yeast-Malt Sprout Extract
3266. Yeasts
3267. Yeasts, Dried
3268. Yellow Prussiate Of Soda
3269. Yerba Santa, Fluid Extract (Eriodictyon Californicum (Hook
3270. Ylang-Ylang, Oil (Cananga Odorata Hook. F. And Thomas)
3271. Yucca, Joshua-Tree (Yucca Brevifolia Engelm.)
3272. Yucca, Mohave, Extract (Yucca Spp.)
3273. Zedoary (Curcuma Zedoaria (Berg.) Rosc.)
3274. Zedoary Bark, Extract (Curcuma Zedoaria (Berg.) Rosc.)
3275. Zein Powder
3276. Zinc Acetate
3277. Zinc Carbonate
3278. Zinc Chloride
3279. Zinc Dithionite
3280. Zinc Gluconate
3281. Zinc Methionine Sulfate
3282. Zinc Oxide
3283. Zinc Stearate
3284. Zinc Sulfate
3285. Zingerone
Table 4: FDA Inactive Ingredient List

Adapted from http://www.fda.gov/cder/igil/igfaqWEB.htm

According to 21 CFR 210.3(b)(8), an inactive ingredient is any component of a drug product other than the active ingredient. Only inactive ingredients in the final dosage forms of drug products are in this database. The Inactive Ingredients Database provides information on inactive ingredients present in FDA-approved drug products. This information can be used by industry as an aid in developing drug products. For new drug development purposes, once an inactive ingredient has appeared in an approved drug product for a particular route of administration, the inactive ingredient is not considered new and may require a less extensive review the next time it is included in a new drug product. For example, if a particular inactive ingredient has been approved in a certain dosage form at a certain potency, a sponsor could consider it safe for use in a similar manner for a similar type of product.

### Ingredient List

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>1,1,1-TRICHLOROETHANE-ORAL; TABLET-000071556-~</td>
</tr>
<tr>
<td>2.</td>
<td>1,1,1-TRICHLOROETHANE-ORAL; TABLET, COATED-000071556-</td>
</tr>
<tr>
<td>3.</td>
<td>1,1,2,2-TETRAFLUOROETHANE-NASAL; SPRAY, METERED-~</td>
</tr>
<tr>
<td>4.</td>
<td>1,2,6-HEXANETRIOL-TOPICAL; EMULSION, CREAM-000106694-<del>7.5-</del></td>
</tr>
<tr>
<td>5.</td>
<td>1,3-DIMETHYLOL-5,5-DIMETHYLHYDANTOIN-TOPICAL; LOTION-006440580-48.4-~</td>
</tr>
<tr>
<td>6.</td>
<td>1-AMINOCYCLOHEXANECARBOXYLIC ACID, C-11-ORAL; CAPSULE-~</td>
</tr>
<tr>
<td>7.</td>
<td>1-METHYL-2-PYRROLIDINONE-PERIODONTAL; DRUG DELIVERY SYSTEM-000672504-~</td>
</tr>
<tr>
<td>8.</td>
<td>1-METHYL-2-PYRROLIDINONE-SUBCUTANEOUS; INJECTION-000872504-25.85-~</td>
</tr>
<tr>
<td>9.</td>
<td>1-O-TOLYLBIGUANIDE-TOPICAL; SOLUTION-000093696-0.0125-~</td>
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<tr>
<td>10.</td>
<td>2-AMINO-2-METHYL-1-PROPANOL-TOPICAL; EMULSION, CREAM-000124685-1-~</td>
</tr>
<tr>
<td>11.</td>
<td>2-AMINO-2-METHYL-1-PROPANOL-TOPICAL; LOTION-000124685-0.3-~</td>
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<tr>
<td>12.</td>
<td>2-NAPHTHOLE SULFONATE SODIUM SALT-ORAL; SUSPENSION-~</td>
</tr>
<tr>
<td>13.</td>
<td>ACACIA-BUCCAL/SUBLINGUAL; TABLET-009000015-9.1-~</td>
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<tr>
<td>14.</td>
<td>ACACIA-ORAL; CAPSULE-008000015-~</td>
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<tr>
<td>15.</td>
<td>ACACIA-ORAL; CAPSULE, SUSTAINED ACTION-009000015-11.77-~</td>
</tr>
<tr>
<td>16.</td>
<td>ACACIA-ORAL; POWDER-009000015-80-~</td>
</tr>
<tr>
<td>17.</td>
<td>ACACIA-ORAL; POWDER, FOR ORAL SUSPENSION-009000015-64.8-~</td>
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<tr>
<td>18.</td>
<td>ACACIA-ORAL; POWDER, FOR ORAL SUSPENSION-009000015-~</td>
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<tr>
<td>19.</td>
<td>ACACIA-ORAL; POWDER, FOR SUSPENSION-009000015-~</td>
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<tr>
<td>20.</td>
<td>ACACIA-ORAL; SYRUP-009000015-~</td>
</tr>
<tr>
<td>21.</td>
<td>ACACIA-ORAL; TABLET-009000015-70-~</td>
</tr>
<tr>
<td>22.</td>
<td>ACACIA-ORAL; TABLET (IMMED./COMP. RELEASE), UNCOATED, CHEWABLE-009000015-80-~</td>
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<tr>
<td>23.</td>
<td>ACACIA-ORAL; TABLET, COATED-009000015-156-~</td>
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<tr>
<td>24.</td>
<td>ACACIA-ORAL; TABLET, DELAYED ACTION, ENTERIC COATED-009000015-10-~</td>
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<tr>
<td>25.</td>
<td>ACACIA-ORAL; TABLET, FILM COATED-009000015-14.9-~</td>
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<tr>
<td>26.</td>
<td>ACACIA-ORAL; TABLET, REPEAT ACTION-009000015-11.542-~</td>
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<tr>
<td>27.</td>
<td>ACACIA-ORAL; TABLET, SUSTAINED ACTION-009000015-34.4-~</td>
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<tr>
<td>28.</td>
<td>ACACIA-ORAL-20; TABLET-009000015-33.5-~</td>
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<td>29.</td>
<td>ACACIA-ORAL-21; TABLET-009000015-5-~</td>
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<td>30.</td>
<td>ACACIA-ORAL-28; TABLET-009000015-5-~</td>
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<tr>
<td>31.</td>
<td>ACACIA MUCILAGE-ORAL; TABLET, COATED-008047389-27.2-~</td>
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<tr>
<td>32.</td>
<td>ACACIA SYRUP-ORAL; CAPSULE, SUSTAINED ACTION-008047387-69.64-~</td>
</tr>
<tr>
<td>33.</td>
<td>ACESULFAME POTASSIUM-BUCCAL; GUM, CHEWING-033665906-2-~</td>
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<tr>
<td>34.</td>
<td>ACESULFAME POTASSIUM-DENTAL; SOLUTION-033665906-0.12-~</td>
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<tr>
<td>35.</td>
<td>ACESULFAME POTASSIUM-ORAL; POWDER, FOR ORAL SOLUTION-033665906-0.117-~</td>
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<tr>
<td>36.</td>
<td>ACESULFAME POTASSIUM-ORAL; POWDER, FOR SUSPENSION-033665906-0.9-~</td>
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<tr>
<td>37.</td>
<td>ACESULFAME POTASSIUM-ORAL; SOLUTION-033665906-0.5-~</td>
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<tr>
<td>38.</td>
<td>ACESULFAME POTASSIUM-ORAL; SUSPENSION, LIQUID-033665906-0.15-~</td>
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<tr>
<td>39.</td>
<td>ACESULFAME POTASSIUM-ORAL; TABLET-033665906-4.4-~</td>
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<tr>
<td>40.</td>
<td>ACESULFAME POTASSIUM-ORAL; TABLET (IMMED./COMP. RELEASE), UNCOATED, CHEWABLE-033665906-2.143-~</td>
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<tr>
<td>41.</td>
<td>ACESULFAME POTASSIUM-ORAL; TABLET, FILM COATED-033665906-8.19-~</td>
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<tr>
<td>42.</td>
<td>ACESULFAME POTASSIUM-SUBLINGUAL; TABLET-033665906-3-~</td>
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<tr>
<td>43.</td>
<td>ACETIC ACID-auricular (otic); SUSPENSION-~</td>
</tr>
<tr>
<td>44.</td>
<td>ACETIC ACID-IM - IV - SC; INJECTION-~</td>
</tr>
<tr>
<td>45.</td>
<td>ACETIC ACID-IM - IV; INJECTION-~</td>
</tr>
</tbody>
</table>
46. ACETIC ACID-IM - SC; INJECTION~~
47. ACETIC ACID-INTRAMUSCULAR; INJECTION~~0.02~% 
48. ACETIC ACID-INTRAVENOUS; INJECTABLE~~0.01~% 
49. ACETIC ACID-INTRAVENOUS; INJECTION~~12.75~% 
50. ACETIC ACID-IV(INFUSION); INJECTION~~1~% 
51. ACETIC ACID-OPHTHALMIC; POWDER, FOR SOLUTION~~
52. ACETIC ACID-OPHTHALMIC; SOLUTION~~0.043~% 
53. ACETIC ACID-ORAL; CAPSULE, SUSTAINED ACTION~~
54. ACETIC ACID-SUBCUTANEOUS; INJECTION~~
55. ACETIC ACID-SUBCUTANEOUS; POWDER, FOR INJECTION SOLUTION, LYOPHILIZED~~
56. ACETIC ACID-SUBCUTANEOUS; SOLUTION, INJECTION~~
57. ACETIC ACID-TOPICAL; SOLUTION~~
58. ACETIC ACID-TOPICAL; SPONGE~~
59. ACETIC ACID-TOPICAL; SUSPENSION~~0.04~% 
60. ACETIC ACID, GLACIAL~AN,ININFILTRATION; INJECTION~~000064197~~
61. ACETIC ACID, GLACIAL~AURICULAR (OTIC); SOLUTION~~000064197~~
62. ACETIC ACID, GLACIAL~AURICULAR (OTIC); SUSPENSION~~000064197~~
63. ACETIC ACID, GLACIAL~AURICULAR (OTIC); SUSPENSION, LIQUID~~000064197~2.55~% 
64. ACETIC ACID, GLACIAL~EXTRACORPOREAL; SOLUTION~~000064197~~
65. ACETIC ACID, GLACIAL~IM - IV - SC; INJECTION~~000064197~0.352~% 
66. ACETIC ACID, GLACIAL~IM - IV - SC; POWDER, FOR INJECTION SOLUTION~~000064197~~
67. ACETIC ACID, GLACIAL~IM - IV; INJECTION~~000064197~0.25~% 
68. ACETIC ACID, GLACIAL~IM - SC; INJECTION~~000064197~0.2~% 
69. ACETIC ACID, GLACIAL~IM - SC; INJECTION, SUSTAINED ACTION~~000064197~~
70. ACETIC ACID, GLACIAL~INTRA-ARTICULAR; INJECTION~~000064197~~
71. ACETIC ACID, GLACIAL~INTRAESIONAL; INJECTION~~000064197~~
72. ACETIC ACID, GLACIAL~INTRAMUSCULAR; INJECTION~~000064197~0.25~% 
73. ACETIC ACID, GLACIAL~INTRASYNOVIAL; INJECTION~~000064197~~
74. ACETIC ACID, GLACIAL~INTRAVENOUS; INJECTABLE~~000064197~0.046~% 
75. ACETIC ACID, GLACIAL~INTRAVENOUS; INJECTION~~000064197~0.36~% 
76. ACETIC ACID, GLACIAL~INTRAVENOUS; SOLUTION, INJECTION~~000064197~0.051~% 
77. ACETIC ACID, GLACIAL~IRRIGATION; SOLUTION~~000064197~~
78. ACETIC ACID, GLACIAL~IV - SC; INJECTION~~000064197~0.2~% 
79. ACETIC ACID, GLACIAL~IV - SC; LIQUID~~000064197~0.2~% 
80. ACETIC ACID, GLACIAL~IV(INFUSION); INJECTION~~000064197~0.44~% 
81. ACETIC ACID, GLACIAL~IV(INFUSION); POWDER, FOR INJECTION SOLUTION, LYOPHILIZED~~000064197~0.27~% 
82. ACETIC ACID, GLACIAL~IV(INFUSION); SOLUTION, INJECTION~~000064197~0.715~% 
83. ACETIC ACID, GLACIAL~NASAL; SOLUTION~~000064197~~
84. ACETIC ACID, GLACIAL~NASAL; SPRAY, METERED~~000064197~~
85. ACETIC ACID, GLACIAL~NERVE BLOCK; INJECTION~~000064197~~
86. ACETIC ACID, GLACIAL~OPHTHALMIC; SOLUTION~~000064197~0.2~% 
87. ACETIC ACID, GLACIAL~OPHTHALMIC; SOLUTION, DROPS~~000064197~0.09~% 
88. ACETIC ACID, GLACIAL~ORAL; CAPSULE~~000064197~~
89. ACETIC ACID, GLACIAL~ORAL; CAPSULE, HARD GELATIN~~000064197~~
90. ACETIC ACID, GLACIAL~ORAL; CONCENTRATE~~000064197~~
91. ACETIC ACID, GLACIAL~ORAL; SOLUTION, ELIXIR~~000064197~0.1087~% 
92. ACETIC ACID, GLACIAL~ORAL; SOLUTION, SYRUP~~000064197~0.1~% 
93. ACETIC ACID, GLACIAL~ORAL; TABLET~~000064197~0.002~MG 
94. ACETIC ACID, GLACIAL~PHOTOPHORESIS; SOLUTION~~000064197~~
95. ACETIC ACID, GLACIAL~SOFT TISSUE; INJECTION~~000064197~~
96. ACETIC ACID, GLACIAL~SUBCUTANEOUS; INJECTION~~000064197~~
97. ACETIC ACID, GLACIAL~SUBCUTANEOUS; LIQUID~~000064197~0.0107~% 
98. ACETIC ACID, GLACIAL~SUBCUTANEOUS; POWDER, FOR INJECTION SOLUTION, LYOPHILIZED~~000064197~0.041~% 
99. ACETIC ACID, GLACIAL~SUBCUTANEOUS; SOLUTION, INJECTION~~000064197~0.11~% 
100. ACETIC ANHYDRIIDE~INTRAVENOUS; INJECTION~~000108247~~
101. ACETIC ANHYDRIIDE~ORAL; TABLET, SUSTAINED ACTION~~000108247~0.11~MG 
102. ACETONE~IMPLANTATION; PELLET~~000067641~~
103. ACETONE~ORAL; GRANULE, FOR SUSPENSION~~000067641~~
104. ACETONE-ORAL; TABLET-000067641
105. ACETONE-ORAL; TABLET, COATED-000067641
106. ACETONE-ORAL; TABLET, SUSTAINED ACTION-000067641
107. ACETONE-ORAL-21; TABLET-000067641
108. ACETONE-TOPICAL; LOTION-000067641-10-%
109. ACETONE-TOPICAL; SHAMPOO-000067641-13-%
110. ACETONE-TOPICAL; SOLUTION-000067641-12.69-%
111. ACETONE SODIUM BISULFITE-AN,CNLK INTRATHecal; INJECTION-000540921
112. ACETONE SODIUM BISULFITE-AN,INFILTRATION; INJECTION-000540921
113. ACETONE SODIUM BISULFITE-DENTAL; INJECTION-000540921
114. ACETONE SODIUM BISULFITE-INHALATION; SOLUTION-000540921-1-0.5003-%
115. ACETONE SODIUM BISULFITE-NERVE BLOCK; INJECTION-000540921
116. ACETOPHENONE-ORAL; CAPSULE, SOFT GELATIN-000098862-0.01-MG
117. ACETYLATED MONOGLYCERIDES-INTRAVENOUS; INJECTION--
118. ACETYLATED MONOGLYCERIDES-ORAL; CAPSULE, EXTENDED RELEASE--2.37-MG
119. ACETYLATED MONOGLYCERIDES-ORAL; CAPSULE, SUSTAINED ACTION--0.593-MG
120. ACETYLATED MONOGLYCERIDES-ORAL; SOLUTION--24-%
121. ACETYLATED MONOGLYCERIDES-ORAL; TABLET--3.74-MG
122. ACETYLATED MONOGLYCERIDES-ORAL; TABLET, COATED--0.28-MG
123. ACETYLATED MONOGLYCERIDES-ORAL; TABLET, DELAYED ACTION, ENTERIC COATED--5.17-MG
124. ACETYLATED MONOGLYCERIDES-ORAL; TABLET, FILM COATED--2.1-MG
125. ACETYLATED MONOGLYCERIDES-ORAL; TABLET, SUSTAINED ACTION--2.48-MG
126. ACETYLGLYCINE-INTRAVENOUS; INJECTION-000516891-0.5-%
127. ACETYLGLYCINE CITRATE-ORAL; CAPSULE--
128. ACETYLGLYCINE CITRATE-ORAL; CAPSULE, ENTERIC COATED PELLETS--7.6-MG
129. ACETYLGLYCINE CITRATE-ORAL; CAPSULE, SUSTAINED ACTION--18.98-MG
130. ACETYLGLYCINE CITRATE-ORAL; TABLET--0.56-MG
131. ACETYLGLYCINE CITRATE-ORAL; TABLET, ENTERIC COATED PARTICLES--18.7-MG
132. ACETYLGLYCINE CITRATE-ORAL; TABLET, SUSTAINED ACTION--57.35-MG
133. ACETYLTRYPTOPHAN-TRANSDERMAL; INJECTION--0.02-%
134. ACRYLATES COPOlyMER-ORAL; TABLET (IMMED./COMP. RELEASE), UNCOATED, CHEWABLE--5.05-MG
135. ACRYLATES COPOlyMER-ORAL; TABLET, EXTENDED RELEASE--14.71-MG
136. ACRYLATES COPOlyMER-ORAL; TABLET, ORALLY DIS/INTEGRATING, DELAYED RELEASE--11.88-MG
137. ACRYLATES COPOlyMER-ORAL; TABLET, SUSTAINED ACTION, COATED--25.18-MG
138. ACRYLATES COPOlyMER-TOPICAL; EMULSION, CREAM--13.6-%
139. ACRYLATES COPOlyMER-TOPICAL; GEL--10-%
140. ACRYLATES COPOlyMER-TRANSDERMAL; FILM, CONTROLLED RELEASE--382.22-MG
141. ACRYLIC ACID HOMOPOLYMER-TRANSDERMAL; FILM, CONTROLLED RELEASE--
142. ACRYLIC ACID/ISOOCYLACRYLATE COPOlyMER-TRANSDERMAL; FILM, CONTROLLED RELEASE--24.5-MG
143. ADCOTE 72A103-TRANSDERMAL; FILM, CONTROLLED RELEASE--16-MG
144. ADCOTE 72A103-TRANSDERMAL; PATCH, CONTROLLED RELEASE--3.99-MG
145. ADHESIVE TAPE-TOPICAL; DISC--
146. ADHESIVE TAPE-TRANSDERMAL; FILM, CONTROLLED RELEASE--127.85-MG
147. ADIPIC ACID-INTRAMUSCULAR; INJECTION-000124049-1-%
148. AEROTEX RESIN 3730-TRANSDERMAL; FILM, CONTROLLED RELEASE--1.9-MG
149. AOAR-ORAL; TABLET-000902180-0.203-MG
150. AIR-INHALATION; GAS--
151. ALANINE-IV(INFUSION); INJECTION-000056417-77-%
152. ALANINE-IV(INFUSION); SOLUTION, INJECTION-000056417-21-%
153. ALBUMIN AGGREGATED-INTRAVENOUS; INJECTION--0.15-%
154. ALBUMIN COLLOIDAL-INTRAVENOUS; POWDER, FOR INJECTION SOLUTION--0.1-%
155. ALBUMIN HUMAN-INTRAVENOUS; INJECTION-9006535-1-%
156. ALBUMIN HUMAN-INTRAVENOUS; POWDER, FOR INJECTION SOLUTION-9006535-1-%
157. ALBUMIN HUMAN-IV(INFUSION); INJECTION-9006535-1-%
158. ALBUMIN HUMAN-IV(INFUSION); POWDER, FOR INJECTION SOLUTION, LYOPHILIZED-9006535-80-%
159. ALBUMIN HUMAN-SUBCUTANEOUS; INJECTABLE-9006535-0.1-%
DEMANDES OU BREVETS VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS COMPREND PLUS D'UN TOME.

CECI EST LE TOME _1_ DE _3_

NOTE: Pour les tomes additionnels, veillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE THAN ONE VOLUME.

THIS IS VOLUME _1_ OF _3_

NOTE: For additional volumes please contact the Canadian Patent Office.
Claims

1. Use of an Exhaled Drug Ingestion Marker (EDIM) for medication adherence monitoring in a subject who has been provided with a labelled medication, said medication comprising a therapeutic agent, a therapeutic agent and a salt, a therapeutic agent and an excipient, or a therapeutic agent and a taggent wherein:

   a) said medication provided to the subject, labelled with said exhaled drug ingestion marker (EDIM) as part of the molecular structure of the therapeutic agent, salt, excipient, or taggent, wherein in the case of the taggent, the taggent generates the EDIM, wherein the EDIM is detectable in exhaled breath of the subject upon metabolism or without metabolism of the therapeutic agent, salt, excipient or taggent wherein at least one portion of the molecular structure of said therapeutic agent, salt, excipient or taggent is labelled with at least one non-ordinary isotope such that said EDIM contains said non-ordinary isotope;

   b) subject’s exhaled breath is sampled and contacted with a sensor able to detect the presence of the EDIM in the sample, whereby the subject’s adherence in taking the medication is determined based on whether the sensor was able to detect the presence of the EDIM in the sample.

2. The use according to claim 1, wherein the EDIM detectable in exhaled breath is volatile, semi-volatile, or non-volatile compound.

3. The use according to claim 2, wherein the EDIM is a Generally Recognized As Safe (GRAS) compound.

4. The use according to claim 1, wherein the EDIM comprises an isotopic compound as a label, wherein the isotopic-labelled EDIM is released and detectable in said exhaled breath upon the metabolism or without the metabolism by the subject of the therapeutic agent, the salt, the excipient or the taggent.

5. The use according to claim 4 wherein the isotope is a non-radioactive isotope.
6. The use according to claim 5 wherein said isotope is deuterium.

7. The use according to claim 1, wherein the sensor is selected from the group consisting of: infrared detection alone, a miniature gas chromatography (mCG) detector coupled to infrared detection capabilities, and a gas chromatograph coupled to a mass spectrometer, GC-MS.

8. An apparatus for medication adherence monitoring in a subject who has been provided with a labelled medication, said medication comprising a therapeutic agent, a therapeutic agent and a salt, a therapeutic agent and an excipient, or a therapeutic agent and a taggart said apparatus adapted to measure an exhaled drug ingestion marker (EDIM) released following provision to said subject of said medication that is labelled with a non-ordinary isotope as part of the molecular structure of the therapeutic agent, salt, excipient, or taggart such that said non-ordinary isotope is included in said EDIM, wherein, in the case of the taggart, the taggart generates the EDIM, wherein the EDIM is detectable in exhaled breath of the subject upon metabolism or without metabolism of the medication such that said apparatus receives a sample of the subject’s exhaled breath following provision of said medication, said apparatus comprising a sensor for contact with the sample of exhaled breath, wherein the sensor is able to detect the presence of the EDIM in the sample, said apparatus further comprising a means for indicating subject adherence in taking the medication based on whether the sensor was able to detect the presence of the EDIM in the sample, wherein the sensor is selected from the group consisting of: infrared detection alone, a miniature gas chromatography (mCG) detector coupled to infrared detection capabilities, and a gas chromatograph coupled to a mass spectrometer, GC-MS.

9. A method for treating a sample obtained from a subject, said sample comprising a sample of exhaled breath from a subject that has been provided with a medication comprising a therapeutic agent, a therapeutic agent and a salt, a therapeutic agent and an excipient, wherein the salt, or the excipient is labelled with a non-ordinary isotope as part of the molecular structure of the therapeutic agent, the salt, or the excipient such that said non-ordinary isotope
is included in an exhaled drug ingestion marker (EDIM), or a therapeutic agent and a tagant, wherein the tagant generates the EDIM, wherein the EDIM is detectable in exhaled breath of the subject upon metabolism or without metabolism of the therapeutic agent, the salt, said method comprising:

a. obtaining a sample of the subject's exhaled breath;
b. applying a sensor to the sample of exhaled breath, wherein the sensor is able to detect the presence of the EDIM in the sample; and
c. determining subject adherence in taking the medication based on whether the sensor was able to detect the presence of the EDIM in the sample.

10. A method for obtaining data reflecting whether a subject is compliant in taking a medication or not, wherein the medication comprising a therapeutic agent, a therapeutic agent and a salt, a therapeutic agent and an excipient or a therapeutic agent and a tagant, wherein the therapeutic agent, the salt, the excipient or the tagant is labelled with a non-ordinary isotope as part of the molecular structure of the therapeutic agent, the salt, or the excipient such that said non-ordinary isotope is included in said EDIM, or wherein the medication comprises a tagant, the tagant generates the EDIM, wherein the EDIM is detectable in exhaled breath of the subject upon metabolism or without metabolism of the therapeutic agent, salt, excipient or tagant, the method comprising:

a. obtaining a sample of the subject's exhaled breath;
b. applying a sensor to the sample of exhaled breath, wherein the sensor is able to detect the presence of the EDIM in the sample; and

c. obtaining data reflecting whether the subject has adhered in taking the medication based on whether the sensor was able to detect the presence of the EDIM in the sample.

11. The use according to claim 1 wherein, furthermore, the corresponding concentration of the therapeutic agent in the blood is determinable based on the concentration of EDIM in breath.
12. The apparatus according to claim 8 further comprising a means for calculating the corresponding concentration of the therapeutic agent in the blood based on the concentration of EDIM in breath.

13. The method of claim 9, further comprising calculating the corresponding concentration of the therapeutic agent in the blood based on the concentration of EDIM in breath.

14. The method of claim 10, further comprising calculating the corresponding concentration of the therapeutic agent in the blood based on the concentration of EDIM in breath.
\[ \text{Ester} \xrightarrow{\text{Esterases}} \ H_2O \rightarrow \text{Carboxylic Acid} + \text{Alcohol} \]
<table>
<thead>
<tr>
<th>R' - OH</th>
<th>Name of Alcohol</th>
<th>CAS Code</th>
<th>Molecular Weight</th>
<th>Physical Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>Methanol (Methyl alcohol)</td>
<td>CAS: 67-56-1</td>
<td>MeOH</td>
<td>32.04</td>
</tr>
<tr>
<td></td>
<td>Ethanol (Ethyl alcohol)</td>
<td>CAS: 64-17-5</td>
<td>C2H5OH</td>
<td>46.07</td>
</tr>
<tr>
<td>HC</td>
<td>1-Propanol (n-propyl alcohol)</td>
<td>CAS: 71-36-3</td>
<td>C3H7OH</td>
<td>60.10</td>
</tr>
<tr>
<td>C2H5</td>
<td>2-Propanol (isopropyl alcohol)</td>
<td>CAS: 62-49-7</td>
<td>C3H7OH</td>
<td>60.10</td>
</tr>
<tr>
<td>HC</td>
<td>1-Butanol (n-butyl alcohol)</td>
<td>CAS: 71-36-3</td>
<td>C4H9OH</td>
<td>74.12</td>
</tr>
<tr>
<td>C2H5</td>
<td>2-Butanol (sec-butyl alcohol)</td>
<td>CAS: 60-00-4</td>
<td>C4H9OH</td>
<td>74.12</td>
</tr>
<tr>
<td>CH3</td>
<td>3-Methyl-1-butanol (isobutyl alcohol)</td>
<td>CAS: 108-87-5</td>
<td>C5H11OH</td>
<td>88.18</td>
</tr>
<tr>
<td>C2H5</td>
<td>2-Methyl-2-propanol (tert-butyl alcohol)</td>
<td>CAS: 92-62-9</td>
<td>C5H11OH</td>
<td>88.18</td>
</tr>
<tr>
<td>C2H5</td>
<td>3-Methyl-1-butanol</td>
<td>CAS: 62-51-5</td>
<td>C5H11OH</td>
<td>88.18</td>
</tr>
<tr>
<td>HC</td>
<td>1-Octanol (Octyl alcohol)</td>
<td>CAS: 211-61-0</td>
<td>C8H17OH</td>
<td>130.20</td>
</tr>
<tr>
<td>C2H5</td>
<td>2-Octanol (iso-octyl alcohol)</td>
<td>CAS: 111-71-8</td>
<td>C8H17OH</td>
<td>130.20</td>
</tr>
<tr>
<td>HC</td>
<td>1-Hexanol (Hexyl alcohol)</td>
<td>CAS: 111-27-3</td>
<td>C6H13OH</td>
<td>100.18</td>
</tr>
</tbody>
</table>

**FIG. 2**
<table>
<thead>
<tr>
<th>Name of Carboxylic Acid</th>
<th>CAS Code</th>
<th>Molecular Weight</th>
<th>Physical Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formic Acid</td>
<td>CAS: 64-18-6</td>
<td>MF: CH₂O₂</td>
<td>BP: 100.2 °C, MP: 8.4 °C, VP: 44.5 torr at 20 °C</td>
</tr>
<tr>
<td>Acetic Acid</td>
<td>CAS: 64-19-7</td>
<td>MF: C₂H₄O₂</td>
<td>BP: 118.1 °C, MP: 16.7 °C, VP: 30.4 torr at 17 °C</td>
</tr>
<tr>
<td>Propionic Acid</td>
<td>CAS: 79-09-4</td>
<td>MF: C₃H₆O₂</td>
<td>BP: 141 °C, MP: -21 °C, VP: 9.0 torr at 37 °C</td>
</tr>
<tr>
<td>Butyric Acid</td>
<td>CAS: 107-92-6</td>
<td>MF: C₄H₈O₂</td>
<td>BP: 163.5 °C, MP: -3.9 °C, VP: 8.8 torr at 20 °C</td>
</tr>
<tr>
<td>2-Methyl butyric acid</td>
<td>CAS: 669-03-7</td>
<td>MF: C₆H₁₀O₂</td>
<td>BP: 176.3 °C, MP: NA, VP: 0.5 torr at 20 °C</td>
</tr>
<tr>
<td>Valeric acid</td>
<td>CAS: 108-33-4</td>
<td>MF: C₅H₁₀O₂</td>
<td>BP: 185 °C, MP: -34.5 °C, VP: 0.15 torr at 20 °C</td>
</tr>
<tr>
<td>Crotonic acid</td>
<td>CAS: 107-93-3</td>
<td>MF: C₅H₈O₂</td>
<td>BP: 189 °C, MP: 71.5 °C, VP: 0.18 torr at 20 °C</td>
</tr>
<tr>
<td>2-Methyl-2-butanonic acid</td>
<td>CAS: 182-63-1</td>
<td>MF: C₅H₁₀O₂</td>
<td>BP: 203 °C, MP: -3.4 °C, VP: 0.2 torr at 20 °C</td>
</tr>
</tbody>
</table>

**FIG. 3**
<table>
<thead>
<tr>
<th>Enzyme Reaction</th>
<th>CYP Reaction</th>
<th>CYP Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-Demethylation</td>
<td>R-OCH₃ → R-OH + CH₃O</td>
<td>1A2, 2A6, 3A4, 2B6, 2C8, 2D6, 2C19, 2C18, 2D6, 2E1</td>
</tr>
<tr>
<td>N-Demethylation</td>
<td>RR'NCH₃ → RR'NH + CH₃O</td>
<td>1A2, 2A6, 3A4, 2B6, 2C8, 2D6, 2C18, 2C19, 2D6, 2E1</td>
</tr>
<tr>
<td>S-Demethylation</td>
<td>RSCH₂ → R-SH + CH₃O</td>
<td>Rare pathway - CYP fractions?</td>
</tr>
</tbody>
</table>

**FIG. 4**

<table>
<thead>
<tr>
<th>Name of Aldhyde</th>
<th>CAS Code</th>
<th>Molecular Formula</th>
<th>Molecular Weight</th>
<th>Physical Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formaldehyde (Formaldehyde)</td>
<td>50-00-0</td>
<td>CH₃O</td>
<td>30.03</td>
<td>BP: 19.5 °C&lt;br&gt;Mp: 80 °C&lt;br&gt;SG: 1.063 g/ml (water = 1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flash Point: 53 °C&lt;br&gt;Vp: 0.000 g/m²</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Water solubility: &gt; 100 g/100 ml (20 °C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Oral rat LD₅₀: 800 mg/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Inhalation rat LC₅₀: 300 mg/m³</td>
</tr>
<tr>
<td>Acetaldehyde (Ethanal, Ethyl Aldhyde)</td>
<td>75-07-0</td>
<td>C₂H₅O</td>
<td>44.05</td>
<td>BP: 21 °C&lt;br&gt;Mp: 72-2.5 °C&lt;br&gt;SG: 0.978 g/ml (water = 1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flash Point: -29 °C (closed cup)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vp: 1422 mm Hg at 37 °C</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Water solubility: microbc</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Oral rat LD₅₀: 1930 mg/kg</td>
</tr>
<tr>
<td>Propionaldehyde (Propenal, Propyl Aldhyde)</td>
<td>122-38-6</td>
<td>C₃H₆O₂</td>
<td>58.08</td>
<td>BP: 49 °C&lt;br&gt;Mp: -23 °C&lt;br&gt;SG: 0.81 g/ml (water = 1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flash Point: &lt; 6 °C (open cup)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vp: 334.8 torr at 20°C</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Water solubility: 20 g/100 ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Inhalation rat LC₅₀: 800 ppm</td>
</tr>
<tr>
<td>Butyraldehyde (Butanal, Butyl Aldhyde)</td>
<td>122-72-8</td>
<td>C₄H₈O</td>
<td>72.11</td>
<td>BP: 74.8 °C&lt;br&gt;Mp: -45 °C&lt;br&gt;SG: 0.8814 g/ml (water = 1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flash Point: -6.67 °C (closed cup)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vp: 91.5 mm Hg at 20°C</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Water solubility: 7.1 (w/v%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Oral rat LD₅₀: 3995 mg/kg</td>
</tr>
</tbody>
</table>

**FIG. 5**
<table>
<thead>
<tr>
<th>THERAPEUTIC DRUG</th>
<th>KEY DESMETHYL METABOLITE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ALGOSETRON</td>
<td>N-desmethyl metabolite of alosetron</td>
</tr>
<tr>
<td>2. ANGONIPINE</td>
<td>N-desmethyl metabolite of angonipine</td>
</tr>
<tr>
<td>3. BIRAMPAN</td>
<td>N-desmethyl metabolite of birampane</td>
</tr>
<tr>
<td>4. CIBRAMOXINE BENZYLATE</td>
<td>N-desmethyl metabolite of cibramoxide</td>
</tr>
<tr>
<td>5. CLOMIPRAMINE</td>
<td>N-desmethyl metabolite of cimicifugine</td>
</tr>
<tr>
<td>6. CLOZAPINE</td>
<td>N-desmethyl metabolite of clozapine</td>
</tr>
<tr>
<td>7. DOPAMINE HYDROCHLORIDE</td>
<td>N-desmethyl metabolite of dopamine</td>
</tr>
<tr>
<td>8. EUNITRIPTAN HYDROCHLORIDE</td>
<td>N-desmethyl metabolite of eunitriptan</td>
</tr>
<tr>
<td>9. ENCAHINE</td>
<td>N-desmethyl metabolite of encainide</td>
</tr>
<tr>
<td>10. ESERINE MAGNUSMUM</td>
<td>N-desmethyl metabolite of eserine</td>
</tr>
<tr>
<td>11. ESORPHINE</td>
<td>N-desmethyl metabolite of esorpine</td>
</tr>
<tr>
<td>12. IFLOXETINE HYDROCHLORIDE</td>
<td>N-desmethyl metabolite of iflooxine</td>
</tr>
<tr>
<td>13. FERGAPRITAN</td>
<td>N-desmethyl metabolite of fergrapitan</td>
</tr>
<tr>
<td>14. GALANTAMINE HYDROCHLORIDE</td>
<td>N-desmethyl metabolite of galantamine</td>
</tr>
<tr>
<td>15. GEPHARINE</td>
<td>N-desmethyl metabolite of gepharine</td>
</tr>
<tr>
<td>16. IMIPRINE Meroxylate</td>
<td>N-desmethyl metabolite of imiprime</td>
</tr>
<tr>
<td>17. INDOMETHACIN</td>
<td>N-desmethyl metabolite of indomethacin</td>
</tr>
<tr>
<td>18. KETOMEPAZOLE</td>
<td>N-desmethyl metabolite of ketomepazol</td>
</tr>
<tr>
<td>19. LEVOFLOXACIN</td>
<td>N-desmethyl metabolite of levofloxacin</td>
</tr>
<tr>
<td>20. METHOTREXITE</td>
<td>N-desmethyl metabolite of methotrexite</td>
</tr>
<tr>
<td>21. METRONIDAZOLE</td>
<td>N-desmethyl metabolite of metronidazole</td>
</tr>
<tr>
<td>22. MIRASPIRINE (systemic)</td>
<td>N-desmethyl metabolite of miraspirine</td>
</tr>
<tr>
<td>23. MOFIDIN</td>
<td>N-desmethyl metabolite of mofidin</td>
</tr>
<tr>
<td>24. NADAMOTRIEN</td>
<td>N-desmethyl metabolite of nadamotriene</td>
</tr>
</tbody>
</table>

FIG. 7A
<table>
<thead>
<tr>
<th>THERAPEUTIC DRUG</th>
<th>KEY DESMETHYL METABOLITE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naproxen</td>
<td>6-O-desmethylnaproxen</td>
</tr>
<tr>
<td>Indatidone</td>
<td>N-desmetylindatidone</td>
</tr>
<tr>
<td>Ofloxacine</td>
<td>3-5% of dose is metabolized to desmethyloxacin</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>N-desmethyloxacpine</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>monodemethylation metabolites</td>
</tr>
<tr>
<td>Oxifloxacin</td>
<td>Desmethyloxacpine</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>desmethyloxacpine</td>
</tr>
<tr>
<td>Quinidine</td>
<td>desmethyloxacpine</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>desmethyloxacpine</td>
</tr>
<tr>
<td>Ranolazine</td>
<td>desmethyloxacpine</td>
</tr>
<tr>
<td>Rosuvastatin Calcium</td>
<td>metabolized in the liver to desmethyloxacpine</td>
</tr>
<tr>
<td>Selegiline</td>
<td>desmethyloxacpine</td>
</tr>
<tr>
<td>Sertraline Hydrochloride Monohydrate</td>
<td>mono- and di-desmethyloxacrine metabolites</td>
</tr>
<tr>
<td>Sildenafil</td>
<td>N-desmethyloxyacrine</td>
</tr>
<tr>
<td>Tamoxifen (Systemic)</td>
<td>N-desmethyloxacrine</td>
</tr>
<tr>
<td>Topotecan Hydrochloride</td>
<td>desmethyloxacrine</td>
</tr>
<tr>
<td>Tramadol Hydrochloride</td>
<td>desmethyloxacrine</td>
</tr>
<tr>
<td>Trimebutinamide</td>
<td>desmethyloxacrine</td>
</tr>
<tr>
<td>Venlafaxine Hydrochloride</td>
<td>desmethyloxacrine</td>
</tr>
<tr>
<td>Zolmitriptan</td>
<td>CYP-1A2 N-desmethyloxacrine</td>
</tr>
<tr>
<td>Zopiclone</td>
<td>inactive N-desmethyloxacrine</td>
</tr>
</tbody>
</table>

**FIG. 7B**
### FIG. 8

<table>
<thead>
<tr>
<th>THERAPEUTIC DRUG</th>
<th>KEY DESETHYL METABOLITE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 AMIODARONE</td>
<td>N-desethyl amiodarone (N-DEA) highly active</td>
</tr>
<tr>
<td>2 BRINZOLAMIDE</td>
<td>accumulation of N-desethyl brinzolamide in red blood cells</td>
</tr>
<tr>
<td>3 DORZOLAMIDE HYDROCHLORIDE</td>
<td>N-desethyl metabolite accumulates in red blood cells</td>
</tr>
<tr>
<td>4 DORZOLAMIDE HYDROCHLORIDE, TIMOLOL MALEATE</td>
<td>N-desethyl metabolite accumulates in erythrocytes.</td>
</tr>
<tr>
<td>6 OXYBUTYNN</td>
<td>Active metabolite N-desethyl-oxybutynin</td>
</tr>
<tr>
<td>6 PIPERACILLIN SODIUM</td>
<td>Piperacillin metabolized to desethyl metabolite</td>
</tr>
</tbody>
</table>

### FIG. 9

<table>
<thead>
<tr>
<th>THERAPEUTIC DRUG</th>
<th>KEY DESPROPYL METABOLITE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 BESIPRINE</td>
<td>N-despropyl-besiprane</td>
</tr>
<tr>
<td>2 DISOPYRAMIDE</td>
<td>N-despropyl-disopyramide</td>
</tr>
<tr>
<td>3 PERGOLIDE</td>
<td>Despropyl pergolide and despropyl pergolide sulfoxide</td>
</tr>
<tr>
<td>4 PROBENCID</td>
<td>Despropyl- probenicid</td>
</tr>
<tr>
<td>5 PROPafenone</td>
<td>N-despropyl-propafenone (NOR-PPF)</td>
</tr>
<tr>
<td>6 PROPIVERINE</td>
<td>Despropyl-propiverine</td>
</tr>
<tr>
<td>7 ROPINIROLE HYDROCHLORIDE</td>
<td>CYP-1A2: major metabolite is N-despropyl ropinrole</td>
</tr>
<tr>
<td>THERAPEUTIC DRUG</td>
<td>KEY DESBUTYL METABOLITE</td>
</tr>
<tr>
<td>------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>1. Acebutolol</td>
<td>extensive hepatic metabolism resulting in the desbutyl amine acetolol</td>
</tr>
<tr>
<td>3. benfluatol (lumefantrine)</td>
<td>Desbutyl-Benfluatol</td>
</tr>
<tr>
<td>4. bumetanide</td>
<td>desbutyl Metabolite of bumetanide</td>
</tr>
<tr>
<td>5. buprenorphine</td>
<td>desbutyl-bupivacaine</td>
</tr>
<tr>
<td>6. docetaxel</td>
<td>primary metabolite of N-desbutyl docetaxel</td>
</tr>
<tr>
<td>7. Levobupivacaine</td>
<td>CYP3A4 catalysis to desbutyl levobupivacaine</td>
</tr>
<tr>
<td>8. Lumefantrine</td>
<td>major metabolite is desbutyl-lumefantrine (CPE)</td>
</tr>
<tr>
<td>9. Taxazolide</td>
<td>desethyl-desbutyl deesterified compound, desbutyl-deesterified compound, desbutyl-desethyl lactone</td>
</tr>
</tbody>
</table>

FIG. 10A

![Butyraldehyde]

Butyraldehyde
(Butanal)

FIG. 10B
FIG. 14

C-H Aliphatic Stretch

O-H Stretch

C-D Aliphatic Stretch

Wavenumbers (cm⁻¹)

FIG. 14
C-H Stretch

Ethanol (CH$_3$-CH$_2$-OH)

Deuterated Ethanol-d5 (CD$_3$-CD$_2$-OH)

Deuterated Ethanol-d2 (CH$_3$-CD$_2$-OH)

C-D Stretch

FIG. 15
FIG. 17

Ethanol-d2 in Breath
Human Breath (vacuum blank)

C-H Stretch

Carbon Dioxide

C-D Stretch
FIG. 18

Carbon Dioxide (subtracted)

C-D Stretch
FIG. 20

CD Stretch: Ethanol-d5

C-D Stretch: Acetaldehyde-d4
FIG. 21

C-D Stretch:
Ethanol-d5 +
Acetaldehyde-d4

CD Stretch:
Ethanol-d5
FIG. 22

C-H Aromatic Stretch

C-D Aromatic Stretch

Benzene (C₆H₆)

13C-labelled Benzene (13C₆H₆)

Deuterated Benzene (C₆D₆)

Wavenumbers [cm⁻¹]
FIG. 23

Acetaldehyde (CH$_3$CHO)

$^{13}$C-labeled Acetaldehyde ($^{13}$CH$_3^{13}$CHO)
FIG. 24
C-D Stretch

Deuterated Acetaldehyde (CD_3CDO)

Deuterated Formaldehyde (CD_2O)

FIG. 25
FIG. 26
FIG. 27
FIG. 28
Aspartame (L-Aspartyl-L-phenylalanine methyl ester)

FIG. 29

Acetylsalicylic Acid (ASA)

FIG. 30
<table>
<thead>
<tr>
<th>Paraben</th>
<th>Molecular Structure</th>
<th>Chemical Properties</th>
<th>Break Protection</th>
<th>Molecular Weight (POHBA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl paraben</td>
<td><img src="image" alt="Methyl paraben" /></td>
<td>CAS: 99-76-3</td>
<td>MP: 65-15</td>
<td>SF: 1.5</td>
</tr>
<tr>
<td>Ethyl paraben</td>
<td><img src="image" alt="Ethyl paraben" /></td>
<td>CAS: 121-47-3</td>
<td>MP: 166.1-166</td>
<td>SF: 1.6</td>
</tr>
<tr>
<td>Propyl paraben</td>
<td><img src="image" alt="Propyl paraben" /></td>
<td>CAS: 3834-17-0</td>
<td>MP: 156.29</td>
<td>SF: 1.5</td>
</tr>
<tr>
<td>Butyl paraben</td>
<td><img src="image" alt="Butyl paraben" /></td>
<td>CAS: 85-54-0</td>
<td>MP: 242-250</td>
<td>SF: 1.5</td>
</tr>
</tbody>
</table>
**FIG. 32**

Clofibrate

Chemical Names

Clofibrate, Ethyl 2-((4-Chlorophenyl)sulfonyl)methyl)phenoxy)acetate

Esterases

\[ \text{H}_2\text{O} \rightarrow \]

Carboxylic Acid Derivative + Ethanol

**FIG. 33**

Esmolol : 4-[2-Hydroxy-3-\{(1-methylethyl)amino\}prooxy]benzenepropenoic acid methyl ester

\[ \text{RBC Arylesterase} \rightarrow \]

Carboxylic Acid Derivative + Methanol
Abbreviations
Procaine, 2-(Diethylamino)ethyl 4-aminobenzoate
PABA, para-aminobenzoic acid

FIG. 34

Pseudocholinesterase

Procaine

H₂O

H₂N

PABA

2-(Diethylamino)-ethanol

FIG. 35

Estersas

H₂C

H₂C

triester NCE

MW = 336.4

H₂C

H₂C

carboxylic acid

n-Propanol

MW = 60.1

Ethanol

MW = 46.1

tert-Butanol

MW = 74.1
FIG. 36

triester NCE
MW = 344.4

Esterases

\[ \text{carboxylic acid} \]

n-Propanol
MW = 60.1

tert-Butanol
MW = 74.1

Ethanol
MW = 46.1

FIG. 37

quadester NCE
MW = 500.67

Esterases

\[ \text{carboxylic acid} \]

n-Propanol
MW = 60.1

tert-Butanol
MW = 74.1

Ethanol
MW = 46.1

n-Pentanol
MW = 80.2
FIG. 38

Verapamil

CYP-3A4

N-Demethylation

Norverapamil

Formaldehyde

FIG. 39

Erythromycin

CYP-3A4

N-Demethylation

N-desmethyl-erythromycin

Formaldehyde
Amiodarone \[\xrightarrow{\text{CYP-3A4}}\] N-Desethyl amiodarone (DEA) + Acetaldehyde

Propafenone \[\xrightarrow{\text{CYP-2D6}}\] N-Despropyl Propafenone + Propionaldehyde (Propanal)

**FIG. 40**

**FIG. 41**
FIG. 42
**FIG. 43**

- Flecainide
  - O-destrifluoroethylation by CYP-2D6
  - Meta-O-destrifluoroethyl flecainide
  - Trifluoroaldehyde

**FIG. 44**

- Codeine (methyl morphine; 7,8-didehydro-4,5-epoxy-3-methoxy-17-methylmorphinan-6-ol)
  - O-demethylation by CYP-2D6
  - Morphine (7,8-didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol)
  - Formaldehyde
**FIG. 45**

Olanzapine \[\xrightarrow{\text{CYP-1A2}}\] N-Desmethylolanzapine + Formaldehyde

**FIG. 46**

Caffeine (1,3,7-trimethylxanthine) \[\xrightarrow{\text{CYP-1A2}}\] 1,7-dimethylxanthine + Formaldehyde
Amphetamine

Phenylacetone + Ammonia

Adenosine Deaminase

FIG. 47

Adenosine
(9-β-D-Ribofuranosyl-9H-purin-6-amine)

Inosine + Ammonia

FIG. 48