

In Reply Refer To:
Mail Stop 412

April 17, 2014

To: GS-W-ALL

From: Donna N. Myers
Chief, Office of Water Quality

Subject: Approval of New USGS Method (O-2440-14) for Human-Use Pharmaceuticals and Related Compounds in Filtered Water by Direct Aqueous Injection—High Performance Liquid Chromatography with Tandem Mass Spectrometry

The Office of Water Quality (OWQ) has approved a new filtered-water analytical method, O-2440-14, National Water Quality Laboratory (NWQL) laboratory schedule (LS) 2440, for the determination of 110 human-use pharmaceuticals and related compounds.

The U.S. Geological Survey (USGS) developed this method to support studies of selected pharmaceuticals in a variety of filtered water-matrix types including groundwater, surface water, drinking water, and wastewater-treatment plant effluent and influent. Field filtration of 40-milliliter samples for LS2440 is preferred, but unfiltered samples can be filtered at the NWQL for an additional charge. All samples are filtered prior to analysis.

All method analytes are determined without sample pre-concentration or isolation using direct injection of an aliquot of the filtered sample onto a high-performance liquid chromatograph/tandem mass spectrometer. Qualitative identification is by multiple-reaction monitoring tandem mass spectrometry. Nineteen deuterium- or carbon-13-labeled isotope-dilution standard (IDS) compounds are added to each sample just prior to analysis and are used for isotope-dilution quantitation. The 19 IDS compounds represent a range of pharmaceuticals and their associated physicochemical properties. For IDS compounds that are exact analogs to the native pharmaceutical or are structurally similar, the use of IDS quantitation automatically corrects the final concentration for any losses in the reported analyte concentration during analysis based on the absolute recovery of IDS compounds. For those compounds where an exact or structurally similar isotopic analog is not available, the IDS corrects for injection or other instrumental variations during analysis. The pharmaceutical IDS compounds also are quantified using a non-pharmaceutical IDS compound, and so the pharmaceutical IDS compounds are used as surrogates to monitor and compare method performance in environmental samples.

For 110 analytes, the method detection limits (U.S. Environmental Protection Agency, 2005) range from 0.45 to 94 ng/L. The interim reporting levels for the 110 analytes range from 2.2 to 200 ng/L.

Field samples are collected using USGS protocols for organic contaminants (section 5.6.1.F of Wilde and others, 2004), and samples are collected and stored in 40-mL VOA vials until analysis.

This method approval process follows the technical procedures specified in OWQ Technical Memorandum 04.01 and the method is described in a USGS Techniques and Methods Report:

Suggested Citation:

Furlong, E.T., Noriega, M.C., Kanagy, C.J., Kanagy, L.K., Coffey, L.J., and Burkhardt, M.R., 2014, Determination of human-use pharmaceuticals in filtered water by direct aqueous injection–high-performance liquid chromatography/tandem mass spectrometry: U.S. Geological Survey Techniques and Methods, book 5, chap. B10.

The report will be made available through the USGS Publications Warehouse.

If you have any questions about the new analytical method, or would like a copy of the report, when it is available, please contact Ed Furlong (efurlong@usgs.gov, 303-236-3941) or Jeff McCoy (jefmccoy@usgs.gov, 303-236-3940).

If you have questions about the method approval process, please contact Donna Myers (dnmyers@usgs.gov, 703-648-5012).

References cited:

Wilde, F.D., Radtke, D.B., Gibs, Jacob, and Iwatsubo, R.T., eds., 2004 with updates through 2009, Processing of water samples (ver. 2.2): U.S. Geological Survey, Techniques of Water-Resources Investigations, book 9, chap. A5, April 2004. (Also available at <http://pubs.water.usgs.gov/twri9A5/>)

U.S. Environmental Protection Agency, 2005, Part 136, Appendix B—Definition and procedure for the determination of the method detection limit—Revision 1.11, *in* Guidelines establishing test procedures for the analysis of pollutants: U.S. Code of Federal Regulations, Title 40, revised as of December 30, 2005, p. 319–322

Table 1. Chemical Abstracts Service Registry Numbers and U.S. Geological Survey parameter codes for each pharmaceutical.

[Chemical Abstracts Service Registry Number (CASRN) ® is a Registered Trademark of the American Chemical Society. Chemical Abstracts Service (CAS) recommends the verification of the CASRNs through CAS Client Services. The five-digit parameter codes are used by the U.S. Geological Survey to uniquely identify a specific constituent or property in the National Water Information System (NWIS) database. API, active pharmaceutical ingredient; NWIS, National Water Information System; NA, not available]

Active pharmaceutical ingredient (API) name ¹	Alternative, brand, or compound names for APIs or API salts used in commercial formulations	Source, use, and other comment	NWIS parameter code	CASRN ²
1,7-Dimethylxanthine	Paraxanthine	Stimulant, metabolite of caffeine	67446	611-59-6
10-Hydroxy-amitriptyline	NA	Degradate of amitriptyline	67995	1159-82-6
Abacavir	Ziagen	Antiviral; reverse transcriptase inhibitor	68022	136470-78-5
Acetaminophen	Paracetamol, Calpol, Panadol	Over-the-counter analgesic, antipyretic	67436	103-90-2
Acyclovir	Aciver, Cyclovir, Herpex, Zovir	Antiviral for treatment of herpes simplex	67484	59277-89-3
Albuterol	Asmol, Proventil, Salbutamol, Ventolin	β2-adrenergic receptor agonist for asthma treatment	67437	18559-94-9
Alprazolam	Alprx, Anxyl, Panix, Xanax	Benzodiazepine used to treat anxiety disorders	68250	28981-97-7
Amitriptyline	Elavil, Tryptizol, Laroxyl, Lentizol, Sarotex	Tricyclic antidepressant	67522	50-48-6
Amphetamine	Adderall, Benzedrine, Dexedrine, Vyvanse	Psychostimulant	67461	300-62-9
Antipyrine	Analgesine, auralgan, azophene, phenazone, phenazon	Prescription analgesic, antipyretic	67477	60-80-0
Atenolol	Atenol, Esatenolol	Beta blocker used for treatment of hypertension	67502	29122-68-7
Atrazine	NA	Herbicide; used in this method to compare performance between compounds and between methods	65065	1912-24-9
Benztropine	Benzatropine, Cogentinol	Anticholinergic used in treatment of Parkinson's disease	67997	86-13-5
Betamethasone	Corson, Dexamethasone	Synthetic glucocorticoid steroid used to treat inflammatory and autoimmune conditions	67485	378-44-9

Bupropion	Wellbutrin, Zyban, Voxra, Budeprion	Antidepressant and smoking cessation aid	67439	34911-55-2
Caffeine	1-methylxanthine, Caffedrine, No Doz	Psychoactive stimulant in coffee, tea, and other preparations	67440	58-08-2
Carbamazepine	Calepsin, Carbelan, Sirtal, Tegretol	Anticonvulsant and mood stabilizer used for epilepsy, bipolar disorder, trigeminal neuralgia	67441	298-46-4
Carisoprodol	Carisoma, Sanoma, Soma	Muscle relaxant	67498	78-44-4
Chlorpheniramine	Chlor-Trimeton, Chloropiril, Haynon, Hayon, Piriton	Over-the-counter antihistamine for relief of allergy symptoms	67497	132-22-9
Cimetidine	Acinil, Gastromet, Tagamet	Histamine H ₂ -receptor antagonist that inhibits production of stomach acid	67442	51481-61-9
Citalopram	Celexa, Nitalapram, Lexapro	Selective serotonin reuptake inhibitor (SSRI) used to treat major depression, anxiety disorders	67505	59729-33-8
Clonidine	Catapress, Catapressan, Duraclont	Antihypertensive	67518	4205-90-7
Codeine	3-methylmorphine, Codicet	Opiate used as analgesic, antitussive, and antidiarrheal	67443	76-57-3
Cotinine	NA	Metabolite of nicotine; tobacco constituent	67444	486-56-6
Dehydronifedipine	NA	Metabolite of the antihypertensive nifedipine	67445	67035-22-7
Desmethyldiltiazem	<i>N</i> -Monodemethyldiltiazem, <i>N</i> -desmethyldiltiazem	Degradate of diltiazem	67999	86408-45-9
Desvenlafaxine	Norvenlafaxine, <i>O</i> -Desmethylvenlafaxine, Pristiq	Antidepressant serotonin-norepinephrine reuptake inhibitor, also major active metabolite of venlafaxine	68251	93413-62-8
Dextromethorphan	DXM	Cough suppressant in over-the-counter cold and cough medications	67468	125-71-3
Diazepam	Diacepin, Faustan, PAX, Valium	Benzodiazepine used to treat anxiety, insomnia, seizures	67499	439-14-5
Diltiazem	Cardizem, <i>cis</i> -diltiazem, Dilatem, Tildiem	Calcium channel blocker used to treat hypertension, angina, some arrhythmias	67519	42399-41-7
Diphenhydramine	Benadryl, Dimedrol, DPH	Antihistamine	67447	58-73-1
Duloxetine	Ariclaim, Cymbalta, Yentreve, Xeristar	Antidepressant; serotonin-norepinephrine reuptake inhibitor	67448	116539-59-4
Erythromycin	Abomacetin, Erycin, Stiemycin,	Macrolide antibiotic	67449	114-07-8

	Theramycin Z			
Ezetimibe	Ezetrol, Zetia	Cholesterol-reducing medication	67487	163222–33–1
Fadrozole	NA	Aromatase inhibitor used for treatment of breast cancer	68012	102676–47–1
Famotidine	Gaster, Gastrofam, Pepcid	Histamine H2-receptor antagonist that inhibits production of stomach acid	68000	76824–35–6
Fenofibrate	Antara, Lipidil, Lofibra, Tricor	Fibrate drug used to reduce cholesterol levels	67489	49562–28–9
Fexofenadine	Allegra, Telfast, Fastofen, Tilfur, Vifas, Telfexo	Terfenadine degradate; an antihistamine used to treat allergies	67510	83799–24–0
Fluconazole	Diflucan, Trican, Alfumet	Triazole antifungal	67478	86386–73–4
Fluoxetine	Fluoxin, Fluval, Nikomed, Prozac, Symbiax	Selective serotonin reuptake inhibitor (SSRI) used to treat major depression, anxiety disorders	67450	54910–89–3
Fluticasone propionate	Flonase, Flovent Flixonase (as the propionate), Veramyst (as the furoate)	Synthetic corticosteroid used to treat asthma and eosinophilic esophagitis	67529	90566–53–3
Fluvoxamine	Fevarin, Luvox	Selective serotonin reuptake inhibitor (SSRI) antidepressant used to treat depression, anxiety disorders	67521	54739–18–3
Glipizide	Digrin, Glucotrol, Melizide, Minidiab, Sucrazide	Sulfonylurea antidiabetic drug	68001	29094–61–9
Glyburide	Diabeta, Daonil, Glibenclamide, Glynase, Micronase	Sulfonylurea antidiabetic drug	68002	10238–21–8
Hydrocodone	Bekadid, Dihydrocodeinone, Multacodin, Panacet, Vicodin	Semi-synthetic opioid, narcotic analgesic and antitussive	67506	125–29–1
Hydrocortisone	Cortisol, Hydrocort	Naturally-produced glucocorticoid hormone used for immunosuppressive and anti-inflammatory effects	67459	50–23–7
Hydroxyzine	Atarax, Equipose, Quies, Tranquizine Vistaril	Antihistamine, sedative	68005	68–88–2
Iminostilbene	Carbamazepine-Related Compound B, Dibenzazepine	Intermediate for manufacture of carbamazepine, tricyclic antidepressants, also degradate	67481	256–96–2

Ketoconazole	Fungoral, Ketoisdin, Nizora, Orifungal M, Panfungol, Xolegel	Antifungal	68014	65277-42-1
Lamivudine	Epivir, Epivir-HBV, Heptovir, Zeffix	Reverse-transcriptase inhibitor used to treat hepatitis-B	68018	134678-17-4
Lidocaine	lignocaine, xylocaine	Topical anesthetic	67462	137-58-6
Loperamide	Dimor, Fortasec, Imodium, Lopex	Opioid antidiarrheal	67515	53179-11-6
Loratadine	Alavert, Claritin, Flonidan	Antihistamine	67488	79794-75-5
Lorazepam	Atavan, Sedazin, Temesta	Benzodiazepine used for its anxiolytic, amnesic, sedative/hypnotic, anticonvulsant, and muscle relaxant effects	67470	846-49-1
Meprobamate	Equanil, Meprospan, Miltown, Placitate	Carbamate derivative used as an anxiolytic	67464	57-53-4
Metaxalone	Skelaxin, Zorane	Muscle relaxant	67504	1665-48-1
Metformin	Diabetase, Glucophage,	Treatment of Type 2 diabetes	67492	657-24-9
Methadone	Amidone, Dolophine, Heptadon, Methadose, Physeptone, Symoron,	Synthetic opioid used as an analgesic and to treat opioid addiction	67500	76-99-3
Methocarbamol	Delaxin, Forbaxin, Parabaxin, Robaxin	Muscle relaxant	67501	532-03-6
Methotrexate	Amethopterin, Extexate, MTX, Rheumatrex	Antimetabolite and antifolate drug used in treatment of cancer	67525	59-05-2
Methyl-1 <i>H</i> -benzotriazole	Tolyltriazole	Corrosion inhibitor; used in this method to compare performance between compounds and between methods	67514	29385-43-1
Metoprolol	Beatrolol, Metocard, Seroken, Spesicor, Toprol	Used to treat cardiovascular disease, especially hypertension	67523	51384-51-1
Morphine	Dolcontin, MS Contin, MSIR, Avinza, Kadian, Oramorph, Roxanol, Kapanol	Opiate used as analgesic	67458	57-27-2
Nadalol	Anabet, Corgard, Corzide, Solgol	Beta blocker used to reduce high blood pressure, migraine headaches, chest pain	68006	42200-33-9
Nevirapine	Viramune	Antiretroviral used to treat HIV-1 infection	68017	129618-40-2
Nicotine	NA	Alkaloid stimulant found in tobacco	67493	54-11-5
Nizatidine	Acinon, Bonacid, Calmaxid,	Acid inhibitor used to treat ulcer and acid	67479	76963-41-2

	Gastrax, Tazac	reflux disease		
Nordiazepam	Calmday, Madar, Nordaz, Praxadium, Stilny	Benzodiazepine drug used to treat anxiety; also active metabolite of diazepam and other benzodiazepine drugs	68252	1088–11–5
Norethindrone	Norethisterone, Norcept	Oral contraceptive component	67434	68–22–4
Norfluoxetine	NA	Active metabolite of fluoxetine	67451	83891–03–6
Norsertaline	Desmethylsetraline, <i>cis-N</i> -desmethylsertraline	Degradate of sertraline	67532	87857–41–8
Norverapamil	NA	Active metabolite of verapamil	68007	67018–85–3
Omeprazole + esomeprazole ³	Esopral, Lucen, Nexium, Prilosec, Sompraz, Zoleri	Proton pump inhibitors used to treat dyspepsia and ulcers	67512	73590–58–6
Orlistat	Alli, Tetrahydrolipstatin, Xenical	Prevents absorption of fat to treat obesity	67490	96829–58–2
Oseltamivir	Fluvir, Tamiflu, Tamvir	Antiviral	67511	196618–13–0
Oxazepam	Alepam, Medopam, Murelax, Noripam, Opamox, Serepax, Sobril	Benzodiazepine used to treat anxiety, insomnia, and alcohol withdrawal	67469	604–75–1
Oxycodone	Dihydrone, Oxycontin, Oxynorm, Pavinal, Remoxy	Opiate used as analgesic and antidiarrheal; also compounded with acetaminophen or other anti-inflammatory drugs such as ibuprofen	67495	76–42–6
Paroxetine	Aropax, Paxil, Seroxat	Selective serotonin reuptake inhibitor (SSRI) antidepressant used to treat depression, obsessive-compulsive disorder, panic disorder, anxiety disorders	67527	61869–08–7
Penciclovir	Denavir, Famciclovir, Vectavir	Antiviral for treatment of herpes infections	68021	39809–25–1
Pentoxifylline	Oxpentifylline, Pentoxil, Trental, Vazofirin	Cardiovascular drug that improves blood flow	67480	6493–05–6
Phenazopyridine	Baridium, Gastracid, Pyrazofen, Pyridiate, Urogesic, Viridium	Used to treat pain, irritation in urinary tract	68008	94–78–0
Phendimetrazine	Antapentan, Bontril, Mephenmetrazine, Sedafamen, Wehless	Stimulant used as an appetite suppressant	67496	634–03–7
Phenytoin	Aleviatin, Denyl, Dilabid, Hidantal, Lepitoin, Sodanton, Zentropil	Antiepileptic for seizures	67466	57–41–0

Piperonyl butoxide	Butacide, Butocide, Butoxide	Pesticide synergist used in lice treatment medications; also used in this method to compare performance between compounds and between methods	67435	51-03-6
Prednisolone	Deltacortenol, Deltacortril, Delta-Cortef, Codelcortone, Cortalone, Meticortelone, Sterolone	Corticosteroid drug used for the treatment of inflammatory and autoimmune conditions, also a metabolite of prednisone	67483	50-24-8
Prednisone	Ancortone, Bicortone, Colisone, Cortidelt, Dacortin, Deltacortisone, Deltacortone, Ultracortene	Synthetic corticosteroid immunosuppressant drug	67467	53-03-2
Promethazine	Dimapp, Diphergan, Fargan, Phenergan, Procit, VallerGINE	Antihistamine, antiemetic, sedative	67524	60-87-7
Propoxyphene	Algafan, Darvocet, Darvon, Detropophyphene, Femadol	Opioid analgesic used for mild pain	68009	469-62-5
Propranolol	Betalong, Innopran XL, Propranolol, Proprasylyt, Reducor	Beta blocker used for treatment of hypertension, tremors	67516	525-66-6
Pseudoephedrine + ephedrine ³	Isoephedrine, Lopac E 3250, Trans-Ephedrine, Sudafed	Appetite suppressant, decongestant, stimulant	67460	90-82-4, 299-42-3
Quinine	Chinin	Antimalarial, bitter flavoring agent, mild antipyretic, and analgesic	68011	130-95-0
Raloxifene	Evista, Keoxafene	Selective estrogen receptor modulator prescribed for osteoporosis	67530	84449-90-1
Ranitidine	Taural, Terposen, Trigger, Ulcex, Ultidine, Zantac	Acid inhibitor used to treat ulcer and acid reflux disease	67452	66357-35-5
Sertraline	Lustral, Zoloft	SSRI antidepressant used to treat depression, obsessive-compulsive disorder, anxiety disorders	67528	79617-96-2
Sitagliptin	Januvia, Xelevia	Antihyperglycemic	67531	486460-32-6
Sulfadimethoxine	Abcid, Agribon, Bactrovet, Omnibon, Pesulfen, Redifal, Sulfamed D	Sulfonamide antibiotic drug	67503	122-11-2
Sulfamethizole	Ayerlucil, Lucosi, Methazol, Microsul, Rufol, Sulfapyelon, Thiosulfil	Sulfonamide antibiotic drug	67476	144-82-1

Sulfamethoxazole	Bactrim, Septrin, Septra, SMZ, SMX	Sulfonamide antibiotic drug	67454	723-46-6
Tamoxifen	Istubal, Nolvadex, Valodex, Zemide	Estrogen receptor agonist used in the treatment of breast cancer	68015	10540-29-1
Temazepam	Crisonar, Euphynos, Gelthix, Levanxol, Remestan, Restoril, Signopam, Tenox	Hypnotic	67471	846-50-4
Theophylline	Elixophyllin, 1,3-Dimethylxanthine, Nuelin, Respbid, Theocin, Uniphyl	Antiasthmatic, diuretic	67494	58-55-9
Thiabendazole	Bioguard, Bovizole, Equizole, Lombristop, Mintezol, Omnizole, Tiabendazole	Parasiticide, fungicide	67455	148-79-8
Tiotropium	Respimat, Spiriva	Bronchodilator used for chronic obstructive pulmonary disease	67508	186691-13-4
Tramadol	Ralivia, Tiparol, Tramadon, Tramal, Tramaliv, Trapidol, Ultram, Zytram	Opiate used as analgesic	67517	27203-92-5
Triamterene	Ademin, Dyrenium, Dytac, Jatropur, Noridil, Pterofen, Taturil, Urocaudal	Diuretic	67475	396-01-0
Trimethoprim	Abaprim, Bactrim, Proloprim, Monotrim, Syraprim, Trimplex, TMP	Antibiotic used in treatment of urinary tract infections	67456	738-70-5
Valacyclovir	Valtrex, Zelitrex	Antiviral for treatment of herpes infections	67507	124832-26-4
Venlafaxine	Effexor, Trevilor, Velafax	Antidepressant; serotonin-norepinephrine reuptake inhibitor	67534	93413-69-5
Verapamil	Bosoptin, Calan, Dilacorran, Isoptin, Vasolan, Verelan	Calcium channel blocker used in the treatment of hypertension, angina pectoris, cardiac arrhythmia	67472	52-53-9
Warfarin	Coumadin, Jantoven, Lawarin, Marevan, Ratron, Rodafarin, Zoocoumarin	Anticoagulant, also used in rodenticides	67457	81-81-2
¹ APIs are listed by United States Adopted Name (American Medical Association, 2012) or International Nonproprietary Name (World Health Organization, 2012). The CASRN listed for each API is for the free API form; salts and complexes of the APIs are often used in formulations (Gerbino, 2005) and typically have different CASRNs.				

² This report contains Chemical Abstracts Service Registry Numbers (CASRN) ®, which is a Registered Trademark of the American Chemical Society. The CASRN online database provides the latest registry number information: http://www.cas.org . Chemical Abstracts Service recommends the verification of the CASRNs through CAS Client Services SM .				
³ Omeprazole is a racemic mixture of two stereoisomers, and esomeprazole is the pure S-stereoisomer of omeprazole and in this analysis cannot be separated by chromatographic or mass spectral characteristics. Similarly, pseudoephedrine and ephedrine are stereoisomers, and in this analysis cannot be separated by chromatographic or mass spectral characteristics.				
Literature Cited				
American Medical Association, 2012, United States adopted names: Chicago, Ill., American Medical Association, accessed October 17, 2012, at				
http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council.page				
World Health Organization, 2012, International nonproprietary names: Geneva, Switzerland, World Health Organization, accessed October 17, 2012, at				
http://www.who.int/medicines/services/inn/en/index.html				
Gerbino, P.P., 2005, Remington—The science and practice of pharmacy (21 ed.): Philadelphia, Pa., Lippincott Williams and Wilkins, 2415 p.				