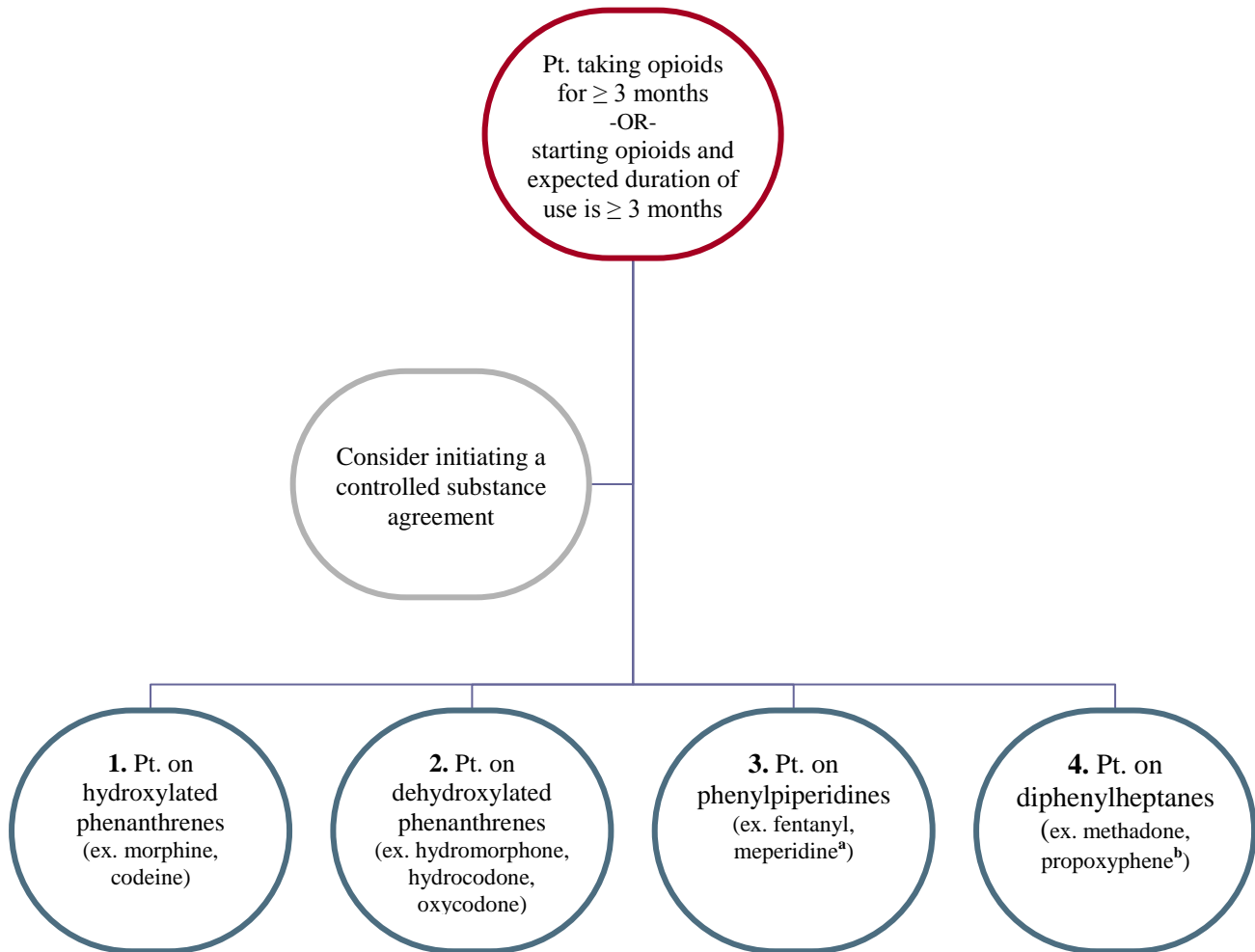


Suggested Urine Drug Screen (UDS) Algorithm

Developed for the Stratton VA Medical Center and affiliated Community Based Outpatient Clinics (CBOCs) in the region encompassing Albany NY

Data collected, collated, and organized by Riham Ywakim, Pharm.D. Candidate.
Reviewed, revised, and reformatted by Dr. Jeffrey Fudin.
Content update by Evan Kujawski, Pharm.D., June 2010

Figure 1: Overall Opioid/Opiate Drug Classifications
Refer to Figure 7 for a complete list of each chemical classification.



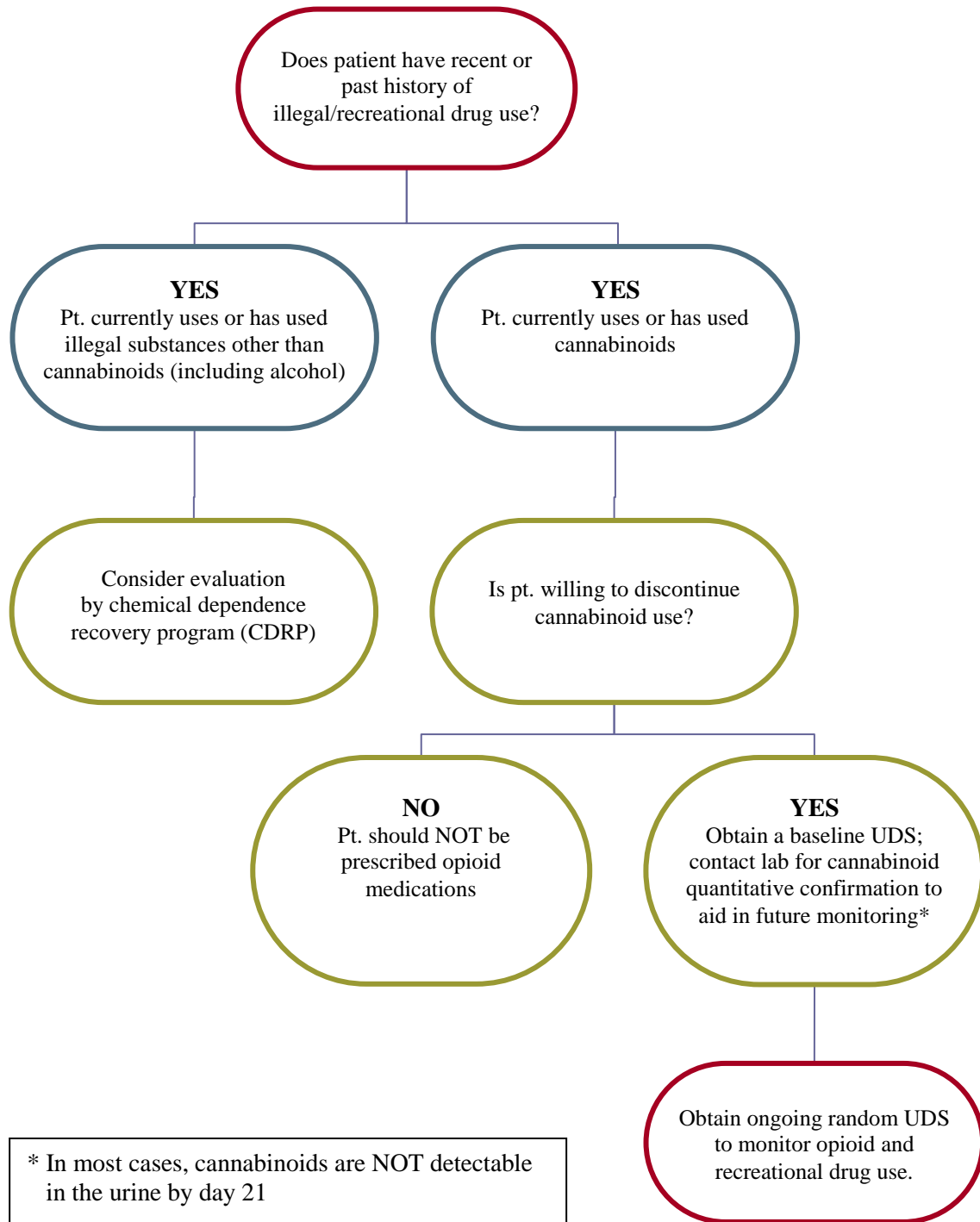
- a. Meperidine should not be used chronically for pain based on toxicity profile.¹
- b. Propoxyphene is a non-formulary drug with marginal analgesic properties and significant toxicity especially in the presence of alcohol use.²

Urine drug screens are intended to **screen** for patients who may be diverting, supplementing, or abusing prescribed drugs or other illicit substances.
They are not intended to predict or determine dose vs. compliance.

1. Raymo LL, Camejo M, Fudin J. Eradicating analgesic use of meperidine in a hospital. *AJHP*. 2007;1150-1153.

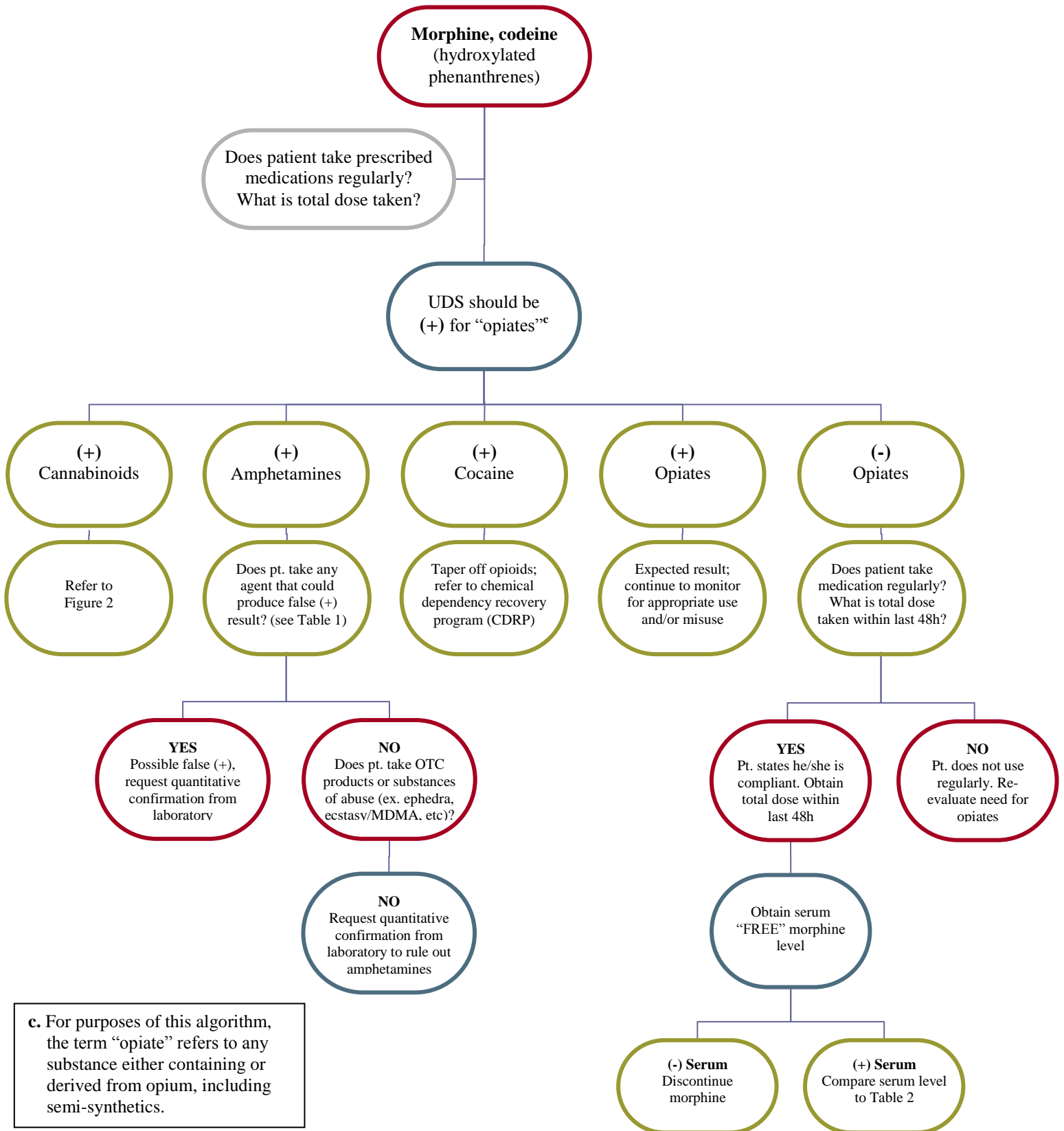
2. Jonasson Ulf, Jonasson B, Saldeen T. Correlation between prescription of various dextropropoxyphene preparations and their involvement in fatal poisonings. *Forensic Science International*. 1999. 103;125-132.

Figure 2: Is your patient a candidate for opioid/opiate medications?



Monitoring Urine Drug Screens

Figure 3: Monitoring UDS for Morphine/Codeine



c. For purposes of this algorithm, the term “opiate” refers to any substance either containing or derived from opium, including semi-synthetics.

Table 1:

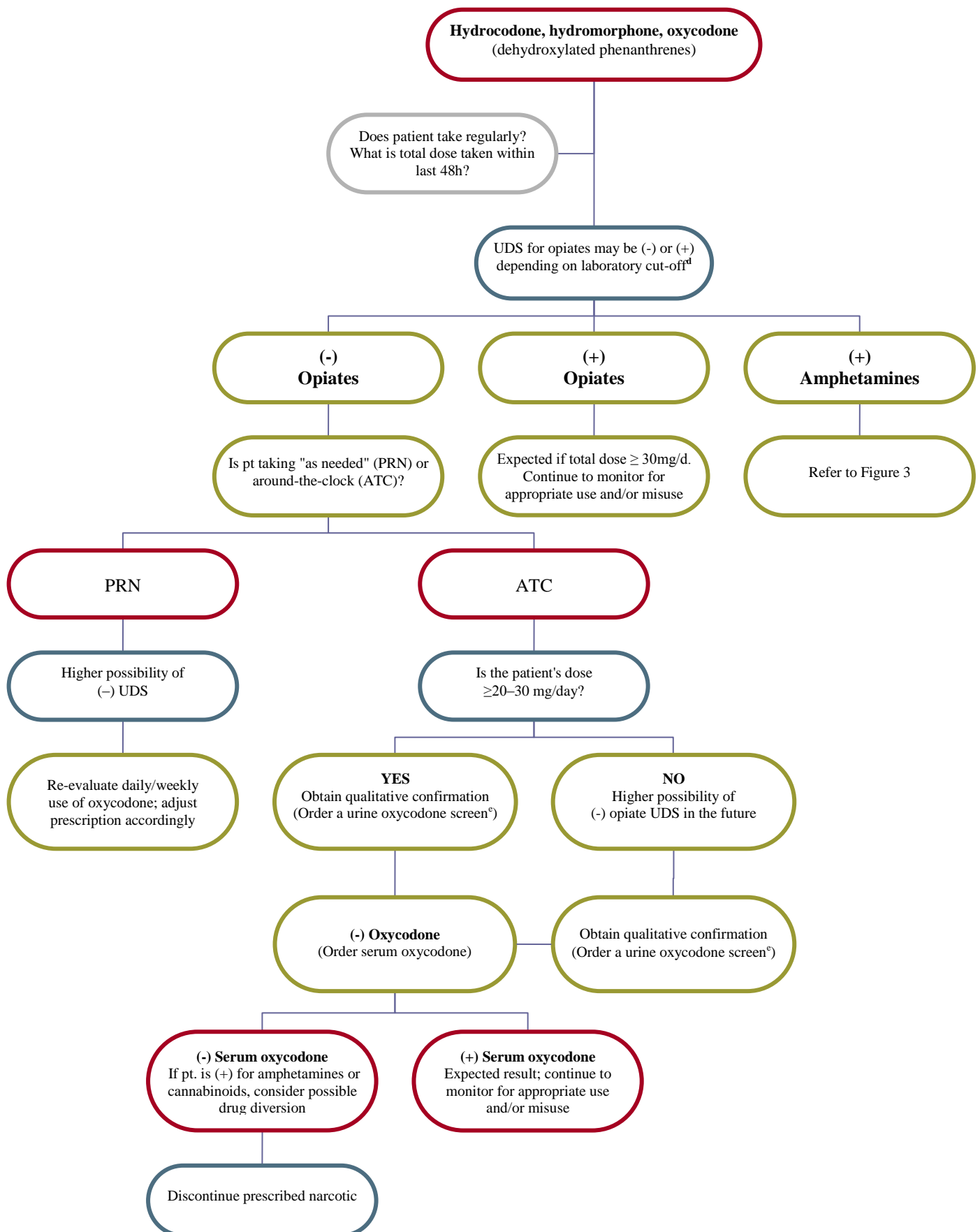
Examples of Drugs that may Cause False Positives for Amphetamines
(Note: This table is not all inclusive)

Any drug with a catecholamine nucleus:

- β -blockers (including propranolol, atenolol, timolol ophthalmic)
- β -agonists
- Dopamine congeners (ex. levadopa, carbidopa, bupropion)
- α -agonist catecholamines [including chronic use of eye drops (Visine®), nasal decongestants (Afrin®)]
- Pseudoephedrine, phenylephrine, ephedra
- Adrenergic ophthalmic (ex. dipivefrin, timolol, levobunolol)

NOTE: Methylphenidate will NOT show (+) for amphetamines

Figure 4: Monitoring UDS for Oxycodone/Hydrocodone/Hydromorphone



d. Stratton VA Medical Center urine opiate cut-off is based on **morphine 300 ng/ml** (outside laboratory detection thresholds may range from 300 to 2000 ng/ml).

The urine **opiate screen** will detect other opiates at the following concentrations:

Oxycodone	23000 ng/mL
Hydrocodone	1700 ng/mL
Hydromorphone	1700 ng/mL
Oxymorphone	41000 ng/mL

e. Urine **oxycodone screen** detection threshold is **100 ng/ml**. This screen offers greater sensitivity versus the standard urine opiate screen (above) for the detection of oxycodone.

The urine oxycodone screen will detect other opiates at the following concentrations:

Hydrocodone	1562 ng/mL
Hydromorphone	12500 ng/mL
Oxymorphone	1562 ng/mL

Please note: The lower the cut-off, the higher the risk for false (+) results; the higher the cut-off, the higher the risk for false (-) results.

Figure 5: Monitoring UDS for Fentanyl

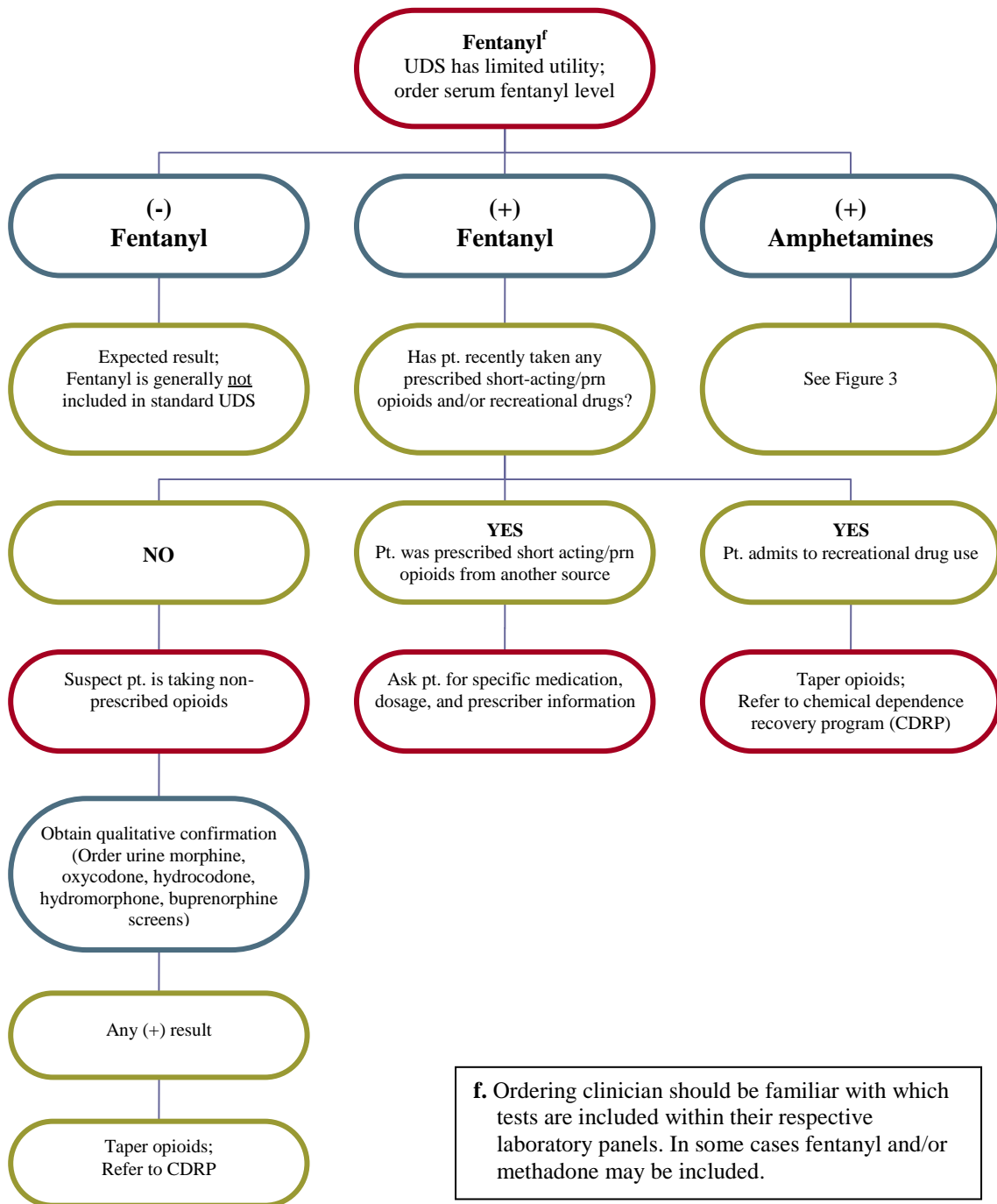
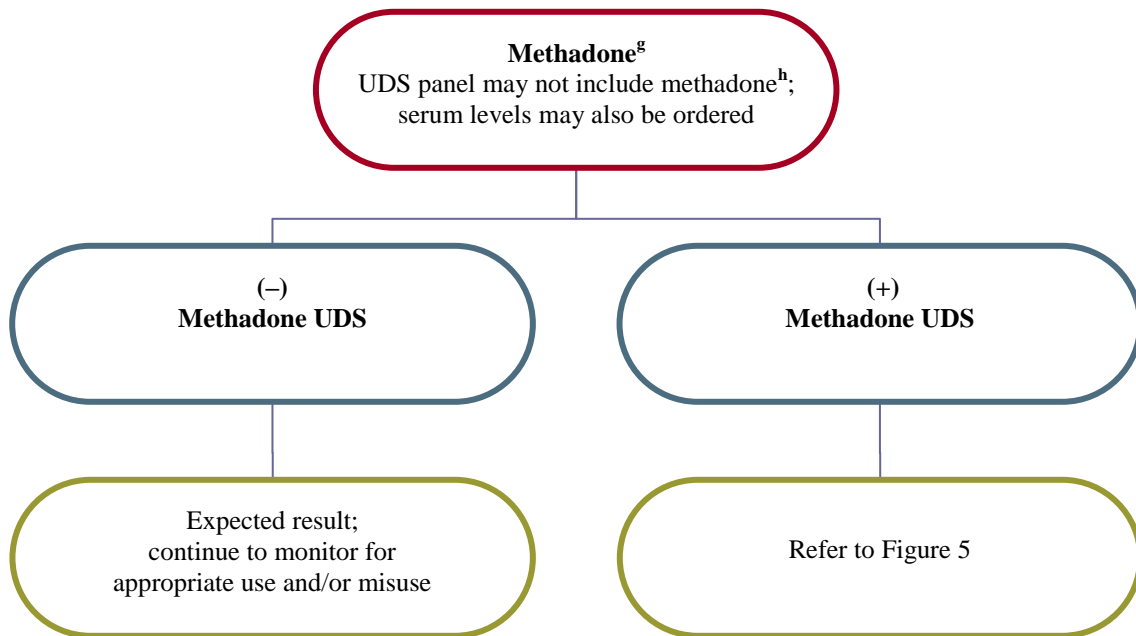


Figure 6: Monitoring UDS for Methadone



g. Methadone is CYP 3A4 substrate and is therefore prone to many drug interactions. Refer to Table 3 for a partial list of CYP 3A4 inhibitors and inducers which have the potential to interact with methadone

h. Stratton VA Medical Center UDS panel includes methadone, but not fentanyl. Methadone UDS may be ordered as a separate test. In some cases fentanyl and/or methadone may be included in the UDS panel (outside of Stratton VAMC). If pt. on $\geq 20\text{mg/d}$ of methadone, urine should remain (+) for 3 days.

Disclaimer: These flow charts are not comprehensive, are not all inclusive, and may not include every possible permutation presented by the patient. These flow charts are intended as a simple guide and ordering clinician MUST know which drugs are included in the urine drug screen panel.

References:

1. Chronic Pain Treatment Guidelines. URL available online at: <http://www.painmed.org/pdf/medical_treatment_utilization_schedule_guidelines.pdf> August 2007 (P: 35-41).
2. Florate Jr, Orlando G. Urinary Drug Testing In Pain Management. Practical Pain Management. PPM Communications, Inc., Glen Mills, PA. April 2005 (P: 38-42).
3. PainEDU.org. Screener and Opioid Assessment for Patients with Pain (SOAPP)®Version 1.0. ©2008 Inflexxion, Inc. URL available online at: http://painedu.org/soapp/SOAPP_24.pdf.
4. Probes, Laerence M. Opioid Blood Levels in Chronic Management. Practical Pain Management. PPM Communications, Inc., Glen Mills, PA. April 2005 (P: 12-18).
5. Veterans Health Administration, Department of Defense. VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. Washington (DC): Veterans Health Administration, Department of Defense; March 2003.
6. Virami, Adil; Mailis, Angela; Shapiro, Lori E; Shear, Neil H. Drug Interactions in Human Neuropathic Pain Pharmacology. © 1997 International Association for the Study of Pain. Pain 73 (1997) 3-13.

Courtesy of Jeffrey Fudin, RPh, BS, PharmD, DAAPM [CPS at Stratton VA Medical Center & Adjunct Associate Professor, Albany College of Pharmacy and Health Sciences (ACPHS)], Riham Ywakim, PharmD Candidate, ACPHS, and Evan Kujawski, RPh, BA, Pharm.D.
Created Aug 2008; updated June 2010.

Table 2

Opioid Pharmacokinetics and Expected Metabolites (Updated 06-2008)

Data updated and revised by Antonio Rivera, Pharm.D. / Reviewed & Reformatted by Jeffrey Fudin, R.Ph., BS, Pharm.D., DAAPM

DRUG	Half-Life (Hrs ^a)	Time to Steady State (Hrs ^a)	Metabolites	Time to Peak Conc. (Hrs ^a)	Serum Predictability	Sample Time After Dose (Hrs ^a)	24 Hour Dose vs. Expected Serum Conc. (ng/mL)
OXYCODONE 1,3,24,28,27	IR=3.2 CR=4.5-8	IR = 17.5 CR = 24-36	Noroxycodone, Oxymorphone, Oxycodyl, Oxymorphol, Noroxycodyl	IR = 1.6 CR = 2.1-3.2	Y	IR = 1.4 +/-0.7 CR = 3.2 +/-2.2	IR 20mg = 15.6 +/-4.4 CR 20mg = 15.1 +/-4.7
MORPHINE 4,5,24,25,26,25	2-4	24	Morphine-3-glucuronide, Morphine-6-glucuronide, Normorphine, Codeine, 7,8-dihydromorphinone	IR = 1 CR = 2-3	Y	IR = 1.0 CR = 4.4	IR 40mg = 11.1 +/-8.4 CR 100mg = 36.9 +/-15.5
TRANSDERMAL FENTANYL 7,8,9,24	16-25	72	Norfentanyl, 4-N-(N-propionylanilino) piperidine, 4-N-(N-hydroxypropionylanilino) piperidine, 1-(2-phenethyl)-4-N-(N-hydroxypropionylanilino) piperidine	24-72	Y	25mcg/hr=38.1hrs 50mcg/hr=34.8hrs 75mcg/hr= 33.5hrs 100mcg/hr=36.8hrs	(600mcg = 0.6 +/-0.3) (1200mcg = 1.4 +/- 0.5) (1800mcg = 1.7 +/- 0.7) (2400mcg = 2.5 +/- 1.2) [XXXXmcg ^g]
HYDROMORPHONE 10,11,12,24,24,24	2.5	12.5	Hydromorphone-3-glucuronide, Hydromorphone-3-glucoside, Dihydroisomorphine-6-glucuronide, Dihydroisomorphine-6-glucoside, Dihydroisomorphine, Dihydromorphine ^f	48-60 min.	Y	IR = 1.47	IR 48 mg = 19.7 +/- 4.04
CODEINE 13,14,24	2.5-3.5	12.5-17.5	Morphine, Norcodeine, Normorphine, Hydrocodone, Codeine 6-glucuronide	1-2	Y	IR = 1.1	IR 180mg = 222.9 +/- 48.9
HYDROCODONE 15,16,17,24,21	3.8-4.5	19-22.5	Hydromorphone, Norcodeine, 6-beta-hydrocodol, 6-alpha-hydrocodol, 6-beta-hydromorphol, 6-alpha-hydromorphol, norhydrocodone	1.3	?	N/A	N/A
METHADONE 18,19,22,24,22	24	~5 days	EDDP (2-ethyl-1,5-dimethyl-3,3-diphenylpyrolinium), EMDP (2-ethyl-5-methyl-3,3-diphenylpyraline)	2-4	Y	SS blood draw @ 24 hr post-dose, before subsequent dose, & after initial dose.	Linear drug levels increase 280ng/mL for every 1mg/kg consumed
HEROIN 21,22,23,24	~3 min. 1.7-5.3 min	~15 min.	6-acetylmorphine, Morphine, Morphine-3-glucuronide, Normorphine, 6-acetylmorphine 3-glucuronide, Normorphine glucuronide	10 minutes for I.M. dose ^h	Y	112mcg/min continuous infusion = 5min ^c	Heroin level = 57 ng/mL ^c 6-acetylmorphine level=15ng/mL ^c
LEVORPHANOL ²⁶	One dose 11-16hr Chronic dosing up to 30 hrs	72hrs	3-glucuronide	approximately 1	?		
PROPOXYPHENE ²⁶	3-12hs		Dextropropoxyphene, nordextropropoxyphene,	2-3			
Meperidine ^{26,27}	~3.6hr	3-6 days	Nomeperidine, meperidinic acid, nomeperidinic acid	1-1.5	?		
Oxymorphone ²² -IR, ER	IR = 7.2 - 9.4hr ER 9.4 - 11.3	IR = 3-4 days ER = 3 days	Oxymorphone-3-glucuronide, 6-OH-oxymorphone,	IR = 30mins ER = 3 hrs	IR=Y? ER=Y		IR ER = linear kinetics have been demonstrated in a dose proportional relationship

IR = Immediate Release Products, CR = Continuous Release products, SS = Steady State
A-Hours, unless otherwise indicated
B-Can detect heroin and 6-acetyl morphine within 10-15 minutes of parenteral administration
C-Administered IV in a single patient over 180 minutes
D-Cumulative amount of fentanyl release from patch dose in 24 hours.
E-hydromorphone is 7,8-dihydromorphinone: Please note that morphine metabolism to hydromorphone has been confirmed in 8 mammals other than humans.
There is only data that correlates the conversion of morphine to hydromorphone in humans.²⁹

Courtesy of Jeffrey Fudin, RPh, BS, PharmD, DAAPM and Antonio Rivera, Pharm.D.

References for Table 2 immediately above and a larger printer friendly version are available online at http://www.paindr.com/2008-06-02_Opioid_Metabolite_Chart_format.pdf

Figure 7

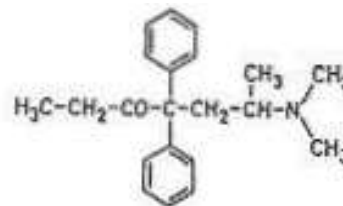
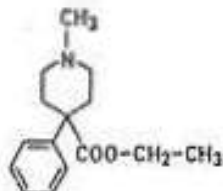
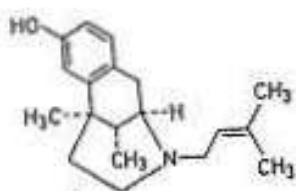
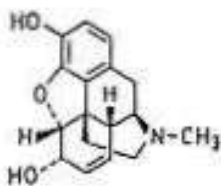
Chemical Classes of Opioids

PHENANTHRENES

BENZOMORPHANS

PHENYLPIPERIDINES

DIPHENYLHEPTANES



**Rx
EXAMPLES:**

MORPHINE

morphine
codeine
hydrocodone*
hydromorphone*
levorphanol*
oxycodone*
oxymorphone*
buprenorphine*
nalbuphine
butorphanol*
naloxone*
heroin (diacetyl-morphine)

PENTAZOCINE

pentazocine
diphenoxylate
loperamide

MEPERIDINE

meperidine
fentanyl
sufentanil
alfentanil
remifentanil

METHADONE

methadone
propoxyphene

X-SENSITIVITY:

PROBABLE

POSSIBLE

LOW RISK

LOW RISK

*These agents lack the 6-OH group of morphine, possibly decreasing cross-sensitivity within the phenanthrene group.

Courtesy of Dr. Jeffrey Fudin (FudinJ@gmail.com)

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Reisine T, Pasternak G. Opioid analgesics and antagonists. In Hardman JG, Limbird LE, Molinoff PB, Ruddon RW, Gilman AG, eds. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 9th ed. New York, NY: McGraw-Hill Companies; 1996:521-555.

Willette RE. Analgesic Agents. In: Wilson and Grisvold's *Textbook of Organic Medicinal Chemistry*. Ninth Edition, Editors: Delgado JN, Remers WA. JB Lippincott Company, Philadelphia, PA. 1991:629-654.

Table 3:

CYP 3A4 Inhibitors and Inducers with the potential to interact with methadone
This table is not all inclusive. Refer questions to a registered pharmacist.

Inhibitors	Inducers
<i>Antidepressants</i>	Carbamazepine
Nefazadone	Dexamethasone
Fluvoxamine	Phenobarbital
Fluoxetine	Phenytoin
Sertraline	Rifampin
Paroxetine	
Venlafaxine	
<i>Azole Antifungals</i>	
Ketoconazole	
Itraconazole	
Fluconazole	
<i>Macrolide Antibiotics</i>	
Clarithromycin	
Erythromycin	
<i>Protease Inhibitors</i>	
Ritonavir	
Saquinavir	
Indinavir	
Nelfinavir	
<i>Others</i>	
Cimetidine	
Diltiazem	

Virami, Adil; Mailis, Angela; Shapiro, Lori E; Shear, Neil H. Drug Interactions in Human Neuropathic Pain Pharmacology. © 1997 International Association for the Study of Pain. Pain 73 (1997) 3-13.

NOTE: Inhibitors will decrease metabolism of substrates and generally lead to increased drug effect. Inducers will increase metabolism of substrates and generally lead to decreased drug effect. Some cytochrome P450 drug interactions have more or less therapeutic significance. Refer questions to a registered pharmacist.

SOAPP® Version 1.0

Name: _____ Date: _____

The following are some questions given to all patients at the Pain Management Center who are on or being considered for opioids for their pain. Please answer each question as honestly as possible. This information is for our records and will remain confidential. Your answers alone will not determine your treatment. Thank you.

Please answer the questions below using the following scale:

0 = Never, 1 = Seldom, 2 = Sometimes, 3 = Often, 4 = Very Often

- | | | | | | |
|---|---|---|---|---|---|
| 1. How often do you feel that your pain is "out of control?" | 0 | 1 | 2 | 3 | 4 |
| 2. How often do you have mood swings? | 0 | 1 | 2 | 3 | 4 |
| 3. How often do you do things that you later regret? | 0 | 1 | 2 | 3 | 4 |
| 4. How often has your family been supportive and encouraging? | 0 | 1 | 2 | 3 | 4 |
| 5. How often have others told you that you have a bad temper? | 0 | 1 | 2 | 3 | 4 |
| 6. Compared with other people, how often have you been in a car accident? | 0 | 1 | 2 | 3 | 4 |
| 7. How often do you smoke a cigarette within an hour after you wake up? | 0 | 1 | 2 | 3 | 4 |
| 8. How often have you felt a need for higher doses of medication to treat your pain? | 0 | 1 | 2 | 3 | 4 |
| 9. How often do you take more medication than you are supposed to? | 0 | 1 | 2 | 3 | 4 |
| 10. How often have any of your family members, including parents and grandparents, had a problem with alcohol or drugs? | 0 | 1 | 2 | 3 | 4 |
| 11. How often have any of your close friends had a problem with alcohol or drugs? | 0 | 1 | 2 | 3 | 4 |

- | | |
|---|-----------|
| 12. How often have others suggested that you have a drug or alcohol problem? | 0 1 2 3 4 |
| 13. How often have you attended an AA or NA meeting? | 0 1 2 3 4 |
| 14. How often have you had a problem getting along with the doctors who prescribed your medicines? | 0 1 2 3 4 |
| 15. How often have you taken medication other than the way that it was prescribed? | 0 1 2 3 4 |
| 16. How often have you been seen by a psychiatrist or a mental health counselor? | 0 1 2 3 4 |
| 17. How often have you been treated for an alcohol or drug problem? | 0 1 2 3 4 |
| 18. How often have your medications been lost or stolen? | 0 1 2 3 4 |
| 19. How often have others expressed concern over your use of medication? | 0 1 2 3 4 |
| 20. How often have you felt a craving for medication? | 0 1 2 3 4 |
| 21. How often has more than one doctor prescribed pain medication for you at the same time? | 0 1 2 3 4 |
| 22. How often have you been asked to give a urine screen for substance abuse? | 0 1 2 3 4 |
| 23. How often have you used illegal drugs (for example, marijuana, cocaine, etc.) in the past five years? | 0 1 2 3 4 |
| 24. How often, in your lifetime, have you had legal problems or been arrested? | 0 1 2 3 4 |

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Available online at: http://painedu.org/soapp/SOAPP_24.pdf