Medicinal Chemistry C

C-2027

1. **DESCRIPTION:** Participants will demonstrate a basic understanding of medicinal chemistry and pharmacology, as well as demonstrate knowledge of various drug pathways and drug syntheses.
   A TEAM OF UP TO: 2 **APPROXIMATE TIME:** 50 minutes
   CALCULATOR: Class II
2. **EVENT PARAMETERS:**
   A. Each team may bring one 8.5" x 11" sheet of paper, which may be in a sheet protector sealed by tape or laminated, that may contain information on both sides in any form and from any source without any affixed labels.
   B. Each team may bring one unmodified and unannotated copy of the official 2027 State Medicinal Chemistry Drug List, but not any other pages of the rules.
   C. Each team may bring up to two Class II calculators.
3. **THE COMPETITION:** The competition will consist of a written examination.
   The written examination will include topics from the following:
   A. *Medicinal chemistry and pharmacology concepts*.
      I. Pharmacodynamics
         a. Bioavailability (including calculating absolute and relative bioavailability given the area under a curve)
         b. Biological half-life
         c. Receptor-ligand binding affinity
         d. Drug efficacy (using dose-response curves)
      II. Pharmacokinetics
         a. Principles of ADME (Absorption, Distribution, Metabolism, Excretion)
         b. Drug delivery systems (e.g., liposomes, antibody-targeted delivery, transmucosal sprays, etc.)
         c. Routes of administration (e.g., oral, intravenous, subcutaneous, etc.)
      III. Drug Discovery
         a. Food and Drug Administration (FDA) Drug Development Process
         b. Assay Plates and Common Analytical Techniques Used
            i. Target-based drug discovery
            ii. Phenotypic drug discovery
            iii. High-throughput screening
            iv. Combinatorial chemistry
   B. *Drug syntheses*. Competitors will be expected to know characteristics of common reactions used in drug syntheses and recognize the same patterns for different substrates and products, as well as the synthesis of specific drugs listed in B-IV. Competitors will be expected to be able to predict the products of given reagents and recognize types of reactions given a reaction scheme, but not the specific mechanism of the reaction. **This section does NOT use the 2027 State Medicinal Chemistry Drug List.**
      I. Common functional group motifs in organic molecules
      II. Carbonyl reactions, Diels-Alder reactions, Suzuki coupling reactions, Friedel-Craft reactions
      III. Functions of common enzymes (e.g., transaminases, isomerases, oxidoreductases, etc.) used in synthetic routes

IV. Drug Synthetic Routes (from precursor to active ingredient)
    a. Naproxen, Aspirin, Ibuprofen, Acetaminophen, Morphine, Codeine, Amphetamine, Lenalidomide, Doxycycline, Lovastatin, Niacin, Ampicillin, Norgestrel, Androgens

C. *Drug mechanisms of action*. Drug and drug classes tested will be limited to the drugs listed in the 2027 State Medicinal Chemistry Drug List. **This is the only section of the rules governed by the 2027 State Medicinal Chemistry Drug List.**
    I. The list has the following format. Note that some drugs are only listed as a generic name due to their generic equivalents being widely prescribed as brand names are discontinued in the United States.

    Category
    Drug Class
    Drug Brand Name (generic name)

    II. Content on each drug is limited to: their drug class, their mechanism of action, the structure of their active ingredient, FDA-approved dosage forms, Drug Enforcement Administration (DEA) Schedule Level (as applicable to controlled substances)
        a. Mechanism of action is specific with respect to the following as applicable:
            i. metabolic pathway (e.g. DNA synthesis, lipid metabolism, etc.)
            ii. neurotransmitter (e.g. gamma-aminobutyric acid, serotonin, dopamine, etc.)
            iii. hormone (e.g. insulin, norepinephrine, angiotensin II, etc.)
            iv. enzyme (e.g. HMG-CoA Reductase, Angiotensin-Converting Enzyme, Cyclooxygenase, etc.)
            v. ion (e.g. sodium, calcium, etc.)

D. The test should be divided so that approximately 20% of points focus on topics under 3.A., 40% focus on topics under 3.B., and 40% focus on topics under 3.C.

4. SCORING:

A. The highest score wins. Points are awarded based on accuracy and quality of detail.
B. Preselected questions will be used as tiebreakers.

5. NOTES TO EVENT SUPERVISORS:

A. Competitors should not, in any way, be expected to make a diagnosis or give a prescription based on a clinical description. The exam should focus strictly on the topics outlined above.
B. Competitors should be able to recognize (i.e. matching, identification of an image, distinguishing functional groups), but not draw, the structures of active ingredients.
C. Competitors should not be expected to know any brand names that are not listed on the 2027 State Medicinal Chemistry Drug List (even if its generic equivalent is listed), side effects, contraindications, or extraneous information (such as the year a drug was patented or average cost, etc.) unless provided as supplementary material in the exam. Upstream and downstream effects of a drug class's direct mechanism of action should only be tested with supplementary material.
    I. Case studies and/or stimulus-based questions are appropriate in the spirit of problem-solving and critical thinking and may contain supplementary information.
D. Competitors should not be tested on medications in only one drug class, but rather there should be an approximately equal distribution of medications tested across every drug class.

6. RECOMMENDED RESOURCES:

A. Note: The parameters of the event are not limited to the content in these recommended resources. However, these may be starting points to serve as foundational knowledge; exam questions must not be directly taken from these resources.
B. Sample mini exam questions for more involved questions: https://tinyurl.com/MedChemCSample
C. Introductory Papers on Pharmacokinetics and Pharmacodynamics
    I. www.ncbi.nlm.nih.gov/books/NBK595006/
    II. publications.ashp.org/display/book/9781585285921/ch01.xml
D. Daily Med FDA-Approved Medication Label Database for basic drug information and mechanisms of action: dailymed.nlm.nih.gov/dailymed/index.cfm
E. PubChem Database for Active Ingredient Information (particularly the "Structures" and "Pharmacology and Biochemistry" sections): pubchem.ncbi.nlm.nih.gov/
F. McMurry's *Organic Chemistry,* 10th edition, available free online via OpenStax: openstax.org/details/books/organic-chemistry

7. SAMPLE QUESTIONS:

Note: It is highly recommended to peruse or attempt the sample mini exam questions in the recommended resources to have an idea of ways that the topics and sample questions would materialize on a test.

1. Identify three drugs with a mechanism of action involving inhibiting cell wall synthesis.
2. Describe how the analytical technique of proteomics is used in phenotypic drug discovery.
3. Identify the characteristics of a reaction catalyzed by a transaminase.
4. Identify one trait common throughout every total synthetic pathway developed in the synthesis of aspirin.
5. Compare and contrast the structures of active ingredients for two different drugs.
    a. Identify functional groups in each compound
    b. Identify the drug that the compound is an active ingredient of and that drug's class
    c. Determine if the drug is a controlled substance as per regulation by the DEA
    d. Identify each drug's drug class and its mechanism of action
6. Refer to your knowledge of the industrial process used to synthesize norgestrel to answer the following questions.
    a. What precursor is commonly used in norgestrel synthesis?
    b. What is the synthetic hormone that is commonly formulated with this precursor?
    c. What catalyst is used to speed up the ethinylation process?
    d. Is it used in catalytic amounts or a stoichiometric amount?
7. Given two reagents and a base catalyst, recognize an aldol reaction and predict the products.
8. Given a table with doses and pharmacological response, calculate the efficacy of a drug at a certain dose.
9. Given the volume of distribution and clearance, calculate the half-life of a drug.
10. Compare the bioavailability of a drug administered in two different routes given the areas under the curve of a concentration vs time graph.
11. Scopolamine (hyoscine) and Zofran (ondansetron) are both antiemetics, which treat nausea and motion sickness. They are often prescribed for postoperative care after chemotherapy or surgery. Scopolamine is often prescribed as transdermal patches and Zofran is often prescribed as tablets.
    a. Compare the routes of administration of a transdermal patch vs a tablet
    b. Relate the principle of absorption to the difference in the routes of administration
    c. Identify the step in the FDA Drug Development Process based on a given scenario

2027 State Medicinal Chemistry Drug List

*: indicates a controlled substance as per regulation by the DEA
**: indicates a drug in which brand name is discontinued and is most prescribed as its generic equivalent

Category
Drug Class
Drug Brand Name (generic name)

Anti-inflammatory Agents
Cyclooxygenase (COX) Inhibitors
Advil (ibuprofen), Bayer Aspirin (aspirin), meloxicam**
Corticosteroids
Deltasone (prednisone), Cortizone (hydrocortisone), Flonase (fluticasone propionate), Pulmicort (budesonide)

Antihistamines
H1 Antihistamines
Zyrtec (cetirizine hydrochloride), Benadryl (diphenhydramine hydrochloride), Claritin (loratadine)
H2 Antihistamines
Pepcid (famotidine)

Digestive Agents
Proton Pump Inhibitors
Prilosec (omeprazole magnesium), Nexium (esomeprazole magnesium), Prevacid (lansoprazole)
Antacids
Tums (calcium carbonate)
Prokinetics
Reglan (metoclopramide hydrochloride)

Lipid-Lowering Agents
3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) Reductase Inhibitors
Lipitor (atorvastatin calcium), Zocor (simvastatin), Crestor (rosuvastatin calcium)

Antidiabetic Agents
Biguanides
metformin**
Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists
Mounjaro (tirzepatide), Ozempic (semaglutide)

Antihypertensives
Angiotensin-Converting Enzyme (ACE) Inhibitors
Vasotec (enalapril maleate), Zestril (lisinopril)
Calcium Channel Blockers
Norvasc (amlodipine besylate), Cardizem (diltiazem hydrochloride)
Thiazide Diuretics
hydrochlorothiazide**

Protein, DNA, and RNA Synthesis Inhibitors
Cephalosporins
cefdinir**, cephalexin**
Fluoroquinolones
Cipro (ciprofloxacin hydrochloride), Avelox (moxifloxacin hydrochloride), Levaquin (levofloxacin)
Macrolide Antibiotics
Zithromax (azithromycin dihydrate), erythromycin**
Antimetabolites
Rasuvo (methotrexate), Droxia (hydroxyurea), Efudex (fluorouracil)
Antifungals
Diflucan (fluconazole), Nizoral (ketoconazole), Lamisil (terbinafine hydrochloride)
Antivirals
Tamiflu (oseltamivir), Zovirax (acyclovir), Valtrex (valacyclovir)

Central Nervous System Agents
Anticonvulsants
Neurontin (gabapentin), Keppra (levetiracetam), Lyrica (pregabalin)*
Benzodiazepines
Xanax (alprazolam)*, Klonopin (clonazepam)*, Ativan (lorazepam)*
Selective Serotonin Reuptake Inhibitors (SSRIs)
Lexapro (escitalopram), Zoloft (sertraline hydrochloride)
Stimulants
Adderall (amphetamine-dextroamphetamine)*, Vyvanse (lisdexamphetamine dimesylate)*