Pacific Northwest
NATIONAL LABORATORY

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Prescription Drug Use in the Workplace

Technical Letter Report

November 2020

Megan E Lerchen
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Prepared for the U.S. Nuclear Regulatory Commission
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Abstract

This report provides an overview of the diverse issues and challenges associated with impairment resulting from prescription medication use and the impact of such impairment on the workforce in safety- and security-sensitive industries. The therapeutic and impairing effects of prescription medication and the current prevailing policy about workplace prescription medication use are described. The defense-in-depth approach inherent in the U.S. Nuclear Regulatory Commission's (NRC's) Fitness for Duty (FFD) requirements for identifying and responding to prescription medication-related impairment that might adversely affect public safety and security are analyzed. This report indicates that for the NRC's FFD programs to effectively address existing and emerging issues associated with prescription drug-related impacts on worker performance and public safety and security, it is important to understand (1) the effects of prescription medicine, (2) the FFD regulations, (3) the licensees' or other entities' workplace drug policy, and (4) covered individuals' responsibilities and rights related to prescription drug use. The report discusses how FFD program implementation depends on consistent, written policy and procedures implemented by a trained workforce and that, for covered individuals, drug effects should be considered in the context of assigned job duties. In addition, key issues for ensuring the continuing effectiveness of FFD programs with respect to prescription medication use are considered, including challenges related to expanding the drug-testing panel, training and education for individuals subject to the FFD rule, and the implications of other relevant Federal laws such as the Americans with Disabilities Act and the Health Insurance Portability and Accountability Act for workplace prescription medication policy.

Acronyms and Abbreviations

AA	access authorization
ADA	Americans with Disabilities Act
ADAAA	Americans with Disabilities Act Amendments Act
AHRQ	Agency for Healthcare Research and Quality
AMA	American Medical Association
AMAS	Aviation Medicine Advisory Service
BJA	Bureau of Justice Assistance
CBER	Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
CNS	central nervous system
CSA	Controlled Substances Act
DEA	Drug Enforcement Agency
DHS	Department of Homeland Security
DoD	U.S. Department of Defense
DOJ	U.S. Department of Justice
DOL	U.S. Department of Labor
DOT	U.S. Department of Transportation
CDT	carbohydrate deficiency transferrin
DRUID	Driving under the Influence of Drugs, Alcohol and Medicine project
EAP	Employee Assistance Program
EEOC	Equal Employment Opportunity Commission
FAA	U.S. Federal Aviation Administration
FD&C Act	(Federal) Food, Drug, and Cosmetic Act
FDA	Food and Drug Administration
FFD	Fitness for Duty
FHWA	Federal Highway Administration
FMCSA	Federal Motor Carrier Safety Administration
FMLA	Family and Medical Leave Act
FRA	Federal Railroad Administration
FTA	Federal Transit Administration
GAO	U.S. Government Accountability Office
HHS	U.S. Department of Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
INN	International Nonproprietary Names
IUPAC	International Union of Pure and Applied Chemistry

LCV	Longer Combination Vehicle
LSBME	Louisiana State Board of Medical Examiners
MRO	medical review officer
MMG	Medicare Model Guidelines
MVC	motor vehicle collision
NAMSDL	National Alliance for Model State Drug Laws
NCCIH	National Center for Complementary and Integrative Health
NCHS	National Center for Health Statistics
NDC	National Drug Code
NHTSA	National Highway Traffic Safety Administration
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NIDA	National Institute on Drug Abuse
NIH	National Institutes of Health
NLM	National Library of Medicine
NPP	nuclear power plant
NRC	U.S. Nuclear Regulatory Commission
NSDUH	National Survey on Drug Use and Health
NTSB	National Transportation and Safety Board
OSHA	Occupational Safety and Health Administration
PDMP	Prescription Drug Monitoring Program
PHMSA	Pipeline and Hazardous Materials Safety Administration
PMP	Prescription (Drug) Monitoring Program
PNNL	Pacific Northwest National Laboratory
PPE	personal protective equipment
SAE	substance abuse expert
SAMHSA	Substance Abuse and Mental Health Services Administration
SAP	substance abuse professional
SME	subject matter expert
SOC	statement of consideration
SSC	structure, system, and component
SSNM	strategic special nuclear material
TRACS	Transit Rail Advisory Committee for Safety
USAN	United States Adopted Names Council
USCG	United States Coast Guard
USP	United States Pharmacopeia
USP-NF	United States Pharmacopeia and National Formulary

Glossary

Term	Definition
abuse	See substance abuse.
anticholinergic	Anticholinergic drugs block (antagonize) the neurotransmitter acetylcholine. Acetylcholine transmits messages for muscle contractions in the body and for learning and memory in the brain. Anticholinergic drugs are used to treat a wide range of health conditions.
covered staff	Employees who are subject to the FFD program. See Appendix D for FFD program applicability to categories of individuals.
misuse	Defined by the CDC as “use in any way not directed by a doctor, including use without a prescription of one’s own medication; use in greater amounts, more often, or longer than told to take a drug; or use in any other way not directed by a doctor” (CDC 2018a) https://www.cdc.gov/drugoverdose/pdf/pubs/2018-cdc-drug-surveillance-report.pdf.
illegal drug	For the purposes of this regulation, any drug that is included in Schedules I to V of Section 202 of the Controlled Substances Act [21 U.S.C. 812], but not when used pursuant to a valid prescription or when used as otherwise authorized by law (10 CFR 26.5).
impairment	Any physiological disorder or condition, cosmetic disfigurement, or anatomical loss affecting one or more body systems, such as neurological, musculoskeletal, special sense organs, respiratory (including speech organs), cardiovascular, reproductive, digestive, genitourinary, immune, circulatory, hemic, lymphatic, skin and endocrine; or any mental or psychological disorder, such as intellectual disability (formerly termed mental retardation), organic brain syndrome, emotional or mental illness, and specific learning disabilities (29 CFR 1630.2(h))
substance abuse	The use, sale, or possession of illegal drugs, or the abuse of prescription and over-the-counter drugs, or the abuse of alcohol (10 CFR 26.5).

Contents

Figures

Tables

1.0 Introduction

A significant portion of the labor force in the United States relies on prescription medication[1] for managing a wide variety of health conditions. While therapeutic, these medications also have side effects, some of which may impair an individual's ability to perform assigned work. This report discusses the impacts and regulation of prescription medication and the interaction among the fitness for duty regulations, workplace drug policy, and individuals' responsibilities and rights related to prescription drug use. This report focuses on safety- and security-sensitive positions within the nuclear workforce. Prescription drug use is a concern because of the diversity of prescribed medications available coupled with the fact that a significant portion of the working age population is medicated and potentially affected by impairing side effects.

The U.S. Nuclear Regulatory Commission (NRC) regulates use of prescription drugs under its Fitness for Duty (FFD) program. The FFD program requires that individuals performing work that potentially affects public health and safety not be under the influence of any substance, legal or illegal, that may impair their ability to perform their duties. Establishing a clear and effective FFD policy for legitimate use of prescription drugs is a critical step in effectively managing a medicated workforce.

This study examines how the broad, coordinated provisions in the FFD program support flexibility in appropriately managing a workforce while considering each covered individual's job duties and health needs. The focus of this report is on legal prescription drug use and, to a lesser extent, misuse of prescription medication. Legal prescription drugs are medications, including controlled substances, obtained through a valid prescription from a qualified and authorized healthcare professional (e.g., a treating physician) for therapeutic purposes consistent with the health condition for which medical treatment is sought. Illegal drug use is outside the scope of this study but is considered where needed in describing the boundaries of legal prescription drug use.

1.1 Background

Prescription medications are widely used to treat a large portion of the U.S. population. A regularly repeated survey by the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics (NCHS) reveals a steady expansion in the prevalence of prescription drug use in the U.S. population and an upward trend in the simultaneous use of multiple prescription drugs. Over the most recent survey period, just under half of the general U.S. population reported prescription drug use in the previous 30-day period, as shown in Table 1.1 (NCHS 2016). The survey results also indicate that prescription drug use increases as the population ages; those aged 65 and older rank the highest and the 45 to 64 age group the second highest across both genders for both single and multiple prescription drug use (see Appendix A for more detail).

[1] Throughout this report, the term prescription drug is used interchangeably with prescription medication. When the general term, drug, is used, it could refer to illegal drugs (e.g., Schedule I controlled substances and street drugs), legally prescribed medication, or over-the-counter medication.

Table 1-1. NCHS survey indicates prescription drug use is common.

	Percentage of population reporting use of prescription drug(s) in the past 30 days		
Surveyed Time Frame	One	Three or More	Five or More
1988-1994	39.1	11.8	4.0
1999-2002	45.2	17.8	7.5
2007-2010	47.5	20.8	10.1
2011-2014	46.9	21.5	10.9

Prescription drug misuse has increased in the past fifteen years (NIDA 2018a).[2] Medications most commonly misused include opioids, central nervous system (CNS) depressants, and stimulants, all of which are all classes of medications identified as controlled substances under the Controlled Substances Act (CSA), Schedules II-IV, and are more likely to be misused in part due to their potential for psychological or physiological dependence in users (SAMHSA 2017).

According to results from the 2017 National Survey on Drug Use and Health reported by the Substance Abuse and Mental Health Services Administration (SAMHSA 2018), an estimated 10 million individuals aged 18 and older misused prescription pain relievers within the past year (SAMHSA 2018[3]). Among the same population, more than five million individuals misused prescription stimulants, more than five million misused tranquilizers, and more than one million misused sedatives. According to another CDC survey, the Annual Surveillance Report of Drug-Related Risks and Outcomes (CDC 2018a, Table 2c),[4] about 91,846,000 individuals, or 34.1% of the surveyed population aged 12 and older, self-reported that they used prescription pain relievers in the past year (i.e., 2015),[5] an estimated 38,756,000 individuals (14.4%) reported using prescription tranquilizers, an estimated 18,420,000 individuals (6.8%) reported using prescription stimulants, and the estimated count of individuals reported to have used prescription sedatives was 18,629,000 (6.9%).

In regulations and medical practice, a variety of terms are used to refer to side effects such as adverse effect, adverse reaction, adverse drug reaction, and adverse event. These terms often are used interchangeably and may or may not have a precise definition. Federal Drug Administration (FDA) regulations at Title 21 of the *Code of Federal Regulations* (CFR) 208.3(k) (21 CFR 208.3(k)) state, "*Serious risk or serious adverse effect* means an adverse drug experience, or the risk of such an experience, as that term is defined in §§ 310.305, 312.32,

[2] Prescription drug misuse is commonly defined as taking a medication without a legitimate prescription that was prescribed for the user and taking or using the medication in a manner that is different than prescribed. See Section 2.4.3 for a more in-depth discussion of misuse (SAMHSA 2017) https://www.samhsa.gov/data/sites/default/files/report_3210/ShortReport-3210.html.

[3] SAMHSA (2018) presents findings from the 2017 National Survey on Drug Use and Health: Detailed Tables. The National Survey presents extensive information on drug, alcohol, and tobacco usage. Tables 1.99A, Table 1.104A, Table 1.109A, and Table 1.114A present usage information on pain relievers, tranquilizers, stimulants, and sedatives, respectively, for the adult population. Note that the tables were dated 2016 and 2017 and the survey questions asked about drug use in the previous year, i.e., 2015 and 2016, respectively (https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHDetailedTabs2017/NSDUHDetailedTabs2017.pdf).

[4] CDC (2018a) includes Table 2c, "2018 Annual Surveillance Report of Drug-Related Risks and Outcomes – United States" (https://www.cdc.gov/drugoverdose/pdf/pubs/2018-cdc-drug-surveillance-report.pdf).

[5] The tables were dated 2016 and the survey questions asked about drug use in the previous year.

314.80, and 600.80 of this chapter." For purposes of this report, the terms "adverse effects," "side effects," and the like include all adverse type effects that could be impairing, and the term "effects" includes both therapeutic and side effects.

Because prescription drug effects can result in an individual's impairment and inability to perform their duties, the NRC has regulations (e.g., 10 CFR Parts 26, 55, and 73) for prescription drug use by covered workers and requires certain nuclear facilities to have FFD programs.[6] NRC regulations further require that these programs provide reasonable assurance that nuclear facility personnel are trustworthy; will perform their tasks in a reliable manner; are not under the influence of any substance, legal or illegal, that may impair their ability to perform their duties; and are not mentally or physically impaired by any cause that can adversely affect their ability to safely and competently perform their duties.

1.2 Overview of Report

The subsequent sections of this report are organized as follows:

- Section 2 discusses prescription drug regulation and explains how to find information about drugs, including their therapeutic and side effects.
- Section 3 describes the FFD program's requirements in FFD-covered facilities and prescription drug use by covered workers.
- Section 4 provides an overview of other federal agencies' prescription drug regulations for safety- and security-related jobs.
- Section 5 discusses other laws that affect the FFD rule implementation (e.g., the Americans with Disabilities Act [ADA], Health Insurance Portability and Accountability Act [HIPAA]).
- Section 6 presents conclusions about and recommendations for FFD program implementation.
- Section 7 provides a bibliography of sources cited in this report.

Many terms regarding prescription drugs and their use may have specific, technical meanings. Refer to the Glossary for definition of selected terms.

[6] In this report, unless otherwise specified, citations are to NRC regulations in Title 10 of the Code of Federal Regulations. For example, the fitness for duty regulations are cited as Part 26 and regulations for the FFD program elements as § 26.21.

2.0 Prescription Drugs Overview

Prescription drugs are substances intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease. They are either chemically manufactured or biologic drug products (made from a living organism or its products or produced by biotechnology methods). They are prescribed by a doctor or another approved healthcare provider, bought at a pharmacy, and are intended to be used by a specific individual.

The NRC's regulations for prescription drug use exist within a larger regulatory framework involving other Federal agencies and organizations that regulate drug naming, approval, information availability, and use, misuse, and abuse. This section provides a high-level look at relevant agencies and organizations and their roles along with background information about prescription drug naming, drug information sources, and drug effects. A detailed look at the NRC's FFD program's oversight of prescription drug use is presented in Section 3.

2.1 Regulators and Standards Organizations

Prescription drugs are highly regulated and under the purview of multiple Federal departments and agencies as well as being within the sanctioned scope of independent organizations. Primary among these is the FDA, which has authority for approving use and overseeing production of each prescription drug. In addition, other agencies within the U.S. Department of Health and Human Services (HHS) and the U.S. Department of Justice (DOJ) also have significant roles in regulatory oversight. An independent organization, the United States Pharmacopeia (USP), also has a long-standing and significant role. See Table 2-1 (next page) for an overview of the roles these organizations play in providing prescription drug oversight. More detailed information about the HHS, DOJ, and USP missions and their roles in the regulatory framework for safe and well-regulated prescription drug use is presented in Appendix B.

2.2 Information Sources

Extensive information about prescription drugs is available from governmental, institutional, and commercial sources. These sources tend to be targeted at specific audiences ranging from consumers to medical practitioners. In all cases, having a drug's name is critical to finding information about that drug.

2.2.1 Drug Names

Prescription drugs can be identified by their assigned chemical, generic, and brand names. Considerable effort and attention go into assigning unique names to drugs to limit the potential for confusion. During the research and development phase, a drug's initial name is simply the name of the chemical compound and typically follows the International Union of Pure and Applied Chemistry (IUPAC) rules for chemical nomenclature. Because the IUPAC names of complex chemicals are usually quite long, the chemical name will often be condensed to a much shorter designation. During the FDA approval process, drug products are assigned unique established (generic) and proprietary (brand) names.

Table 2-1. Role of selected entities in prescription drug oversight.

Entity	Role
U.S. Department of Health and Human Services (HHS)	
Food and Drug Administration (FDA)	FDA is responsible for approving drug products, maintaining lists of drug products, and establishing mandated drug labeling information.
Substance Abuse and Mental Health Services Administration (SAMHSA)	SAMHSA's mission is to reduce the impact of substance abuse on America's communities.
Centers for Disease Control and Prevention (CDC)	CDC protects the public health of the nation by providing leadership and direction in the prevention and control of diseases and other preventable conditions and responding to public health emergencies. CDC tracks prescription drug use rates.
Centers for Medicare & Medicaid Services (CMS)	Responsible for Medicare and Medicaid, including insurer formularies based on commonly prescribed prescription drugs.
National Institutes of Health (NIH) • National Institute on Drug Abuse (NIDA) • National Library of Medicine (NLM)	NIH's organization includes NIDA and NLM. NIDA supports basic research on drug use and addiction. NLM maintains the world's largest biomedical library.
Agency for Healthcare Research and Quality (AHRQ)	AHRQ collects medical expenditure information, including drug usage data about prescribed medicine purchases, to support evidence-based research on healthcare.
U.S. Department of Justice (DOJ)	
Drug Enforcement Agency (DEA)	DEA enforces the controlled substances laws and regulations of the United States.
Bureau of Justice Assistance (BJA)	BJA provides support to state, local, and tribal governments to reduce drug-related crime. This includes activities targeted at opioid abuse and state-run prescription drug monitoring programs.
The United States Pharmacopeia (USP)	
United States Pharmacopeia (USP)	USP sets standards for the identity, strength, quality, and purity of medicines manufactured, distributed, and consumed in the United States.

Generic drug names can be used by any company. In the United States, generic names are established by the United States Adopted Names (USAN) Council based on pharmacological and/or chemical relationships under the authority of 21 CFR 299.4. The USAN Council is a private organization sponsored by the American Medical Association (AMA), the USP, and the American Pharmacists Association. Generic drug names are submitted by the manufacturer and selected through a negotiated process by the USAN Council, which is harmonized with the World Health Organization for International Nonproprietary Names (INN; AMA 2018). When the proposed name is acceptable to the USAN Council, the manufacturer, and the INN Expert Committee, it then becomes an adopted USAN generic name (historically, there have been some differences in establishing approved drug names). A cumulative list of USAN adopted (generic) drug names is published by USP.

Proprietary (also known as brand, trademark, or trade) names are exclusive to each prescription drug and company. The drug sponsor proposes a desired proprietary name to FDA as part of an

FDA application (FDA 2014; FDA n.d.).[7] FDA evaluates proposed proprietary names for acceptability. The proposed name should have limited potential to confuse the new drug with established drug products already in the marketplace and pending products currently under review. Proposed proprietary names may also be found unacceptable if FDA determines a name would promote the drug product (e.g., misleadingly implies unique effectiveness or composition, overstates efficacy, minimizes risk, or claims superiority), represents a potential source of medication error, or other factor that could lead to its misuse. Note that proprietary names for a medication are inconsistent between companies and may be inconsistent between countries for the same drug from the same company.

2.2.2 On-line Resources

Information sources for prescription drugs are numerous, but many of them are designed to meet specific information needs of particular users, require substantial background knowledge, or require a paid subscription. Relatively accessible and complete on-line consumer information resources are:

- MedlinePlus®, an information source published by the NIH's National Library of Medicine: https://medlineplus.gov/
- Prescriber's Digital Reference (PDR, formerly Physician's Desk Reference), an on-line version of the PDR: https://www.pdr.net/.

Other selected resources for prescription drug information, including the FDA resources briefly discussed below in Section 2.3.1, are listed in Appendix C.

2.3 Drug Classification

Drug classification systems are complex. Further, multiple drug classification systems are in use, depending on the reason for their classification. Approaches to pharmaceutical classification are typically based on common characteristics, such as the following:

- therapeutic use/drug indication – based on the conditions the drug treats
- mechanism of action – based on the biochemical reaction to the drug
- mode of action – based on the body's response to the drug
- chemical structure – based on the drug's molecular structure
- potential for abuse – based on the drug's effect(s) and potential for user addiction.

Classification systems may use multiple characteristics or just focus on a subset of drugs; e.g., those with a potential for causing user addiction. Further, depending on the classification system and the drug's properties, drugs can be classified into one or more categories or may not be included in a potentially applicable category. Finasteride is an example of a drug that is captured in two classifications because it is FDA-approved for both enlarged prostate treatment and to regrow hair (FDA 2016a). In contrast, pharmaceutical drugs may be used off-label—using an FDA-approved drug for an unapproved disease or condition—and thus may not be captured in a therapeutic use classification. An example of this is the FDA-approved hypothyroidism drug levothyroxine that is also used for off-label depression treatment (Joffe 2011).

[7] Drug sponsors are the companies, research institutions, and other organizations that take responsibility for developing a drug.

Given the large number of prescription drugs and the multiple possible ways to categorize them, there are many prescription drug classification systems in use. The following sections focus on selected prescription drug classification systems in use by government agencies or mandated by law or regulation.

2.3.1 Food and Drug Administration

The FDA's regulatory authority over drugs is very broad and includes registration and approvals (Junod 2018). The FDA defines the pharmacologic class based on any one of the following three attributes (FDA 2009):

- mechanism of action – pharmacologic action at the receptor, membrane, or tissue level
- physiologic effect (PE) – pharmacologic effect at the organ, system, or whole-body level
- chemical structure.

FDA guidance on drug labeling and drug classes is listed on their website (FDA 2013). For drugs with an established FDA pharmacologic class, the label must state, "(Drug) is a (name of class) indicated for (indication(s))" in accordance with 21 CFR 201.57(a)(6). For example, levothyroxine's drug information from MedlinePlus fulfills this requirement with the statement:

> Levothyroxine is used to treat hypothyroidism (condition where the thyroid gland does not produce enough thyroid hormone). It is also used with surgery and radioactive iodine therapy to treat thyroid cancer. Levothyroxine is in a class of medications called hormones (MedlinePlus 2019).

Note that this description does not include the off-label use of levothyroxine for depression.

Information about FDA-registered drug products and approved prescription drugs is available in several ways. Three major FDA drug information sources are as follows:

- National Drug Code Directory – lists all drug products along with their individual, assigned National Drug Code
- Drugs@FDA database – provides a catalog of extensive information about most of the drug products approved since 1939
- Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) – tracks therapeutic equivalents (i.e., generic drugs).

Additional information about these and other sources is presented in Appendix C. The Federal Food, Drug, and Cosmetic Act (FD&C Act) requires drug establishments (manufacturers, processors, and distributors) to register and list all prescription drugs, active pharmaceutical ingredients, over-the-counter drugs, and homeopathic drugs for commercial distribution in the United States with the FDA.[8,9] The FDA registration information is maintained current through annual updates that are mandatory for drug establishments. Registered drug products are identified and reported using a unique, three-segment number, called the National Drug Code (NDC). The NDC serves as a universal product identifier for drugs. FDA maintains information

[8] Section 510 of the Federal Food, Drug, and Cosmetic Act (Act) (21 U.S.C. § 360); FDA regulations for requirements related to registration and listing are found at 21 CFR § 207.
[9] Foods, dietary supplements, drug intermediates (substances used in the manufacture of active ingredients), and inactive ingredients are excluded from registration requirements.

submitted by the drug establishments about each drug in the publicly available NDC Directory, in which 123,866 drug products were listed as of December 18, 2018.[10] The NDC Directory lists basic information for each drug product, including the NDC number, various names (e.g., proprietary, generic), dosage and delivery information, labeler name, and reference to the drug product's FDA application number. For most of the medications listed, the NDC Directory includes multiple drug products for various forms and doses.[11]

The Drugs@FDA database covers brand name, generic prescription, and over-the-counter human drugs and biological therapeutic products (some therapeutic biological products are excluded). This database catalogs most of the drug products approved since 1939. For drugs approved after 1998, the database provides the majority of available patient information, labels, approval letters, reviews, and other information. The Drugs@FDA database can be used to find

- approved labels for approved drug products
- generic drug products for an innovator (aka brand name) drug product
- therapeutically equivalent drug products for an innovator or generic drug product
- patient information for drugs approved from 1998 on all drugs that have a specific active ingredient
- FDA approval history, including approval letter(s) and review packages about a drug.

The on-line version of the Drugs@FDA database is updated daily. The entire Drugs@FDA database can be downloaded from FDA but downloading does not include the on-line tools for querying or otherwise manipulating the data that are available through the on-line version.[12] FDA cautions that search results from the Drugs@FDA database,

> … are not always related in terms of their chemical makeup or the conditions they treat, and are not necessarily substitutable. They appear together because their drug names or active ingredient names contain the words or parts of words … entered in the search box.

The FDA's publication *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the Orange Book) catalogs therapeutic equivalents between approved prescription drugs and other drug products (e.g., biologics and over-the-counter drugs). Any drug product included in the Orange Book has been approved by the FDA and has not been withdrawn for safety or efficacy reasons. The Orange Book is intended to be used to find generic drug product equivalents but it also provides related patent and exclusivity information. FDA provides on-line access for searching approved drug products in the Orange Book Database by active ingredient, proprietary name, applicant, application number, dosage form, route of administration, or patent number. FDA updates Orange Book information on the current list of approved generic drug products daily while other information is processed and reported in regular monthly updates. The Orange Book and monthly updates can be downloaded from the

[10] The FDA cautions that drugs being listed in the Drug Registration and Listing System does not denote approval by the FDA of the firm or any of its marketed products, nor is it a determination that a product is a drug as defined by the Act, nor does it denote that a product is covered by or eligible for reimbursement by Medicare, Medicaid, or other payers.

[11] The current National Drug Code Directory, *Drug Approvals and Database*, is available at https://www.fda.gov/Drugs/InformationOnDrugs/ucm142438.htm.

[12] The current Drugs@FDA Data Files under Drug Approvals and Databases are available at https://www.fda.gov/Drugs/InformationOnDrugs/ucm079750.htm

FDA website.[13] Note that all of the drugs listed in the Orange Book are included in the Drugs@FDA database, but the Drugs@FDA database includes information that is not in the Orange Book. The two information sources also have different user interface features in their on-line forms.

2.3.2 USP Formulary

USP has two classification systems of interest, one is tied to Medicare and the other is an extension for other uses. Both systems use pharmacotherapeutic evidence in the context of FDA-approved indications to create categories and classes (42 CFR Part 423.100):

- USP Category – the broadest classification; provides a high-level formulary structure designed to include all potential therapeutic agents for diseases and conditions of Medicare Part D beneficiaries.
- USP Class – more granular classification; occurs within a specific USP Category in the USP Model Guidelines, which provides for therapeutic or pharmacologic groupings of FDA-approved medications, consistent with current U.S. healthcare practices and standards of care.

Generally, a drug may appear in more than one USP Category or USP Class if there is a scientifically valid and clinically meaningful patient care issue. Combination drugs, and specific dosage forms, formulations, or delivery systems, are generally not listed but may be included in the associated list if there is a scientifically valid and clinically meaningful patient care issue.

One classification system was created under provisions of the Medicare Prescription Drug Improvement and Modernization Act of 2003 (Section 1860D-4(b)(3)(C)(ii)). In this classification system–the USP Medicare Model Guidelines (MMG)–the HHS Centers for Medicare and Medicaid Services entered cooperative agreements with USP to develop and maintain a list of categories and classes for use by insurers in their formularies for Medicare Part D drugs (drugs not on the Medicare Part D formulary are excluded).[14]

USP's other classification system is the USP Drug Classification, which was developed in response to stakeholder input requesting a classification system beyond the MMG to assist with formulary support outside of Medicare Part D. The USP Drug Classification is intended for drug classification during formulary development or review. While the USP Drug Classification is extensive, it is not comprehensive and USP notes specifically that the USP Drug Classification does not include all drugs administered in a clinical setting (USP n.d.).

2.3.3 DEA-Controlled Substance Schedules

The DOJ's DEA maintains the schedules of controlled substances required under the CSA. Drugs are categorized in the schedules based on whether they have a currently accepted medical use in treatment in the U.S., their relative abuse potential, and likelihood of causing dependence when abused. Schedule I controlled substances by definition have no medical use and have the highest potential for user abuse and dependence, while Schedule V drugs have

[13] The current FDA Orange Book (Approved Drug Products with Therapeutic Equivalence Evaluations) is available at https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book.

[14] Medicare requires that drug plans offer at least two drugs in the most commonly prescribed categories and classes.

the lowest. Purchase and use of medications in Schedules II–V require a prescription involving a real doctor-patient relationship (DEA n.d.-b).

An updated and complete list of the DEA schedules is published annually in 21 CFR Parts 1308.11 through 1308.15. DEA also maintains an electronically available list of controlled substances known as the Orange Book (not to be confused with the FDA Orange Book described in Section 2.3.1 and Appendix C) (DEA 2019).

Note that under provisions of the Controlled Substance Analogue Enforcement Act (21 U.S.C. §§ 802(32) and 813), unscheduled analogs of controlled substances in Schedules I or II are treated as controlled substances in Schedule I for purposes of control and prosecution.[15] This provision provides enforcement and control authority for otherwise unregulated designer drugs that mimic the pharmacological effects of the controlled substance. It is also important to note that DEA's lists

> …describe the basic or parent chemical and do not describe the salts, isomers, salts of isomers, esters, ethers, and derivatives which may be controlled substances. These are not comprehensive lists so please note that a substance need not be listed as a controlled substance to be treated as a scheduled substance for criminal prosecution (DEA 2019).

2.4 Prescription Drug Usage and Effects

As mentioned previously, prescription drug use is prevalent in the United States—about half the population of working age adults reported prescription drug use. The CDC's annual *Health, United States* reports on national health status and trends, including data about the number of prescription drugs used and percentage of the population using selected prescription drug classes in the past 30 days (CDC 2018c). Based on these data, overall consumption of prescription drugs has been trending upward since the late 1980s and individuals tend to increase the number of prescription drugs they take as they get older. For the 2011 to 2014 period, 37.1% of individuals aged 18–44 years and 69.0% of individuals aged 45–64 years reported taking at least one prescription drug in the previous 30 days. Additional selected data about prescription drug usage for working age adults from the CDC report are presented in Appendix A.

2.4.1 Therapeutic and Side Effects

Drugs approved by the FDA for sale in the United States must be safe (the benefits of the drug must be greater than its known risks) and effective (the drug must have the purported therapeutic effect) (FDA 2019a). Prescription drugs are taken for their therapeutic effects. However, most drugs also have side effects in addition to their primary desired effects. Whether side effects manifest is complex and depends on the drug's action and the body's response. Further, taking more than one drug might exacerbate each drug's side effects or result in adverse effects that would not occur with either drug alone. Some side effects are unwanted, uncomfortable, or dangerous. Side effects can vary from minor problems like a runny nose to life-threatening events, such as an increased risk of a heart attack. Either or both therapeutic and side effects may cause impairment that could affect an individual's fitness for duty. Further,

[15] An analog is a compound that has a molecular structure similar to another structure (in this case, a scheduled drug).

an individual may be taking a prescription drug to treat an underlying condition that in itself may impair an individual's ability to safely perform his or her job duties.

According to the FDA (2018a), side effects can be initiated when an individual

- starts taking a new drug
- stops taking a drug that the individual has been on for a while
- increases or decreases the drug's dosage.

Whether any of a drug's adverse effects manifest depend on multiple factors, including age, gender, allergies, drug absorption, and interaction with other drugs, food, vitamins, and dietary supplements. Because the severity of any side effect depends on the prescription drug and the individual's response, the same side effect may be impairing in one individual but not in another. Drug side effects vary in their probability of occurrence and severity of impact. The duration of a drug's adverse effects and the severity of its impairment depend on the drug and the individual.

Common side effects include upset stomach, nausea, skin irritation (itching, rash), muscle aches, dry mouth, dizziness, slowed movement, fainting, drowsiness, and inability to focus or pay attention. For many drugs, there is a period of time needed to develop tolerance to the drug so that side effects are no longer experienced. In some cases, a medication's dose can be adjusted to optimize the therapeutic effect and minimize the side effects to tolerable levels. For some drugs, the chemical structure of the drug combined with the human metabolism assures that a specific side effect is unavoidable. The first-generation antihistamines such as diphenhydramine (brand name Benadryl, available in over-the-counter and prescription formulations) are a good example of this because, while blocking the allergic response, they also cause drowsiness by interfering with sleep regulation (Lie et al. 2015).

For most prescription medications, there will be a long list of potential adverse effects. When taken as prescribed, drug side effects can be roughly categorized as

- limited or unnoticeable,
- noticeable, and
- work affecting.

Predicting whether and how long an individual will experience an adverse effect can be difficult. For each drug or combination of drugs the side effect(s) may vary, as follows:

- The side effect may not manifest.
- The side effect may be temporary and go away given adjustments to the drug regime or the individual's tolerance to the drug.
- The side effect may be unavoidable and may last until the individual no longer takes the drug.
- The side effect may be permanent and may endure after the individual no longer takes the drug.

For drugs that have intolerable side effects, a medical professional may suggest lowering the dosage, switching to a different drug, adding another drug (e.g., anti-nausea medication), changing the time at which one takes a medication (e.g., taking a drug that causes dizziness at bedtime rather than with breakfast), controlling conditions or exposures to other factors (e.g., limiting sun exposure while taking Accutane to avoid skin damage), or making lifestyle changes to remove the need for the medication (e.g., losing weight to lower cholesterol rather than taking

a statin). In some cases, prescription drugs are recommended for medical treatment despite the intolerable side effects when there is no other better option (e.g., cancer chemotherapy). There may also be some cases where the adverse effect an individual could experience is potentially worse than the anticipated therapeutic effect, driving a need to explore other treatment options. For example, the insomnia drug Ambien (zolpidem) can also cause dizziness, vision problems, daytime drowsiness, sleepwalking, mental/mood problems, kidney or liver disease, and other adverse effects.

Information about side effects is available from prescription labels (which include patient inserts), FDA databases, NLM resources, manufacturers and distributors, and other resources (see Section 2.2.2). This information is collected during the drug's development and approval processes and may be updated based on new information collected by the FDA after the drug is available to consumers (FDA 2016b).[16] FDA regulations require that prescription drug label information about the drug's effects include the following:[17]

- A list of adverse reactions. This section must list the adverse reactions that occur with the drug and with drugs in the same pharmacologically active and chemically related class, if applicable. The list(s) must be preceded by the information necessary to interpret the adverse reactions (e.g., for clinical trials, total number exposed, extent and nature of exposure).
- Categorization of adverse reactions. In a list, adverse reactions must be categorized by body system, severity of the reaction, or in order of decreasing frequency, or by a combination of these, as appropriate. Within a category, adverse reactions must be listed in decreasing order of frequency. If frequency information cannot be reliably determined, adverse reactions must be listed in decreasing order of severity.
- Comparisons of adverse reactions between drugs. For drug products other than biological products, any claim comparing the drug to which the labeling applies with other drugs in terms of frequency, severity, or character of adverse reactions must be based on adequate and well-controlled studies unless this requirement is waived. For biological products, any such claim must be based on substantial evidence.

For an individual picking up a prescription drug at the pharmacy, the amount of information provided can be overwhelming and impairment warnings may be poorly understood (National Academies of Sciences, Engineering, and Medicine 2015; Pollini et al. 2017). The medical community encourages individuals to talk to a healthcare professional, such as a primary care provider or pharmacist, to ensure that warnings are understood, review patient insert information, or query on-line resources that provide drug information (see Section 2.2.2) (FDA 2018a).

[16] Once a drug is on the market, the FDA continues surveillance and risk assessment programs to identify adverse events that did not appear during the drug approval process and updates drug labeling and, rarely, reevaluates the drug approval or marketing decision (FDA 2016b).

[17] Per FDA regulations at 21 CFR 201.57(c)(7), "For purposes of prescription drug labeling, an adverse reaction is an undesirable effect, reasonably associated with use of a drug, that may occur as part of the pharmacological action of the drug or may be unpredictable in its occurrence. This definition does not include all adverse events observed during use of a drug, only those adverse events for which there is some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event."

2.4.2 Drug Interactions

A drug interaction happens when another substance affects the activity of a drug. This other substance could be another drug, food, alcohol, vitamin or supplement, or another ingested or absorbed material such as an essential oil. The other substance may increase or reduce the effect of a drug through action or interference. Sometimes it may cause a completely different effect to occur. Types of drug interactions along with representative examples include the following:

- Drug-drug: Using more than one medication at a time may result in exacerbating side effects or triggering new side effects. For example, aspirin and warfarin are both blood thinners and have a compounding effect when consumed together (MedlinePlus 2017).
- Drug-alcohol: Mixing alcohol with prescription drugs often exacerbates the risk of adverse events, including the degradation of cognitive and mechanical capability caused by alcohol alone (NIAAA 2014).
- Drug-food: Grapefruit and grapefruit juice interfere with enzymes that metabolize more than 85 medications, including increasing the length of time statins stay in the body, leading to increased risk for liver and muscle damage (Bailey et al. 2013).
- Drug-herb: St. John's wort decreases the effect of many drugs by speeding up cytochrome P-450 metabolization and intestinal P-glycoprotein cellular transport of multiple drugs including the immunosuppressant drug cyclosporine, the antiretroviral agent indinavir, oral contraceptives, coumadin, digoxin, and benzodiazepines (NCCIH 2015).

To minimize or avoid adverse drug interactions, individuals are counseled to consult with their physician or pharmacist about their medications, review patient insert information, or query on-line resources that provide drug interaction information (see Section 2.2.2).

For some conditions, combination therapies have been developed that rely on multiple drugs that have collective, often synergistic effects that provide a more effective treatment than use of individual medications.[18] Combination therapies that rely on multiple drugs are often referred to as drug cocktails and are used for a variety of conditions, including infectious diseases and metabolic, cardiovascular, autoimmune, and neurological disorders. The benefits of pursuing combination therapies include improving the treatment effectiveness with drugs that involve multiple metabolic pathways, reducing side effects by using lower doses of individual drugs, and reducing the potential for developing drug resistance. The extensive ongoing research into combination therapies will undoubtedly lead to increasing prevalence of drug cocktails (Nature Medicine 2017).

2.4.3 Misuse and Abuse

A review of the medical and mental health literature reveals varying definitions of prescription drug "misuse" and prescription drug "abuse." Some of the definitions also overlap. There is more consistency and agreement regarding the definition of prescription drug "abuse" than prescription drug "misuse" (see Table 2-2 for a high-level overview). However, the prevailing consensus is that these terms have distinct meanings, which is consistent with the NRC's use of these terms, as described in 10 CFR Part 26 and in the Statement of Considerations (SOC) for the final rulemaking (NRC 2008).

[18] Combination therapy may also include other therapies such as biologic (immunotherapy), psychological, or physical.

The NRC's definition of prescription drug "abuse" defined in 10 CFR Part 26 and in the SOC for the final rulemaking (NRC 2008) is found under NRC's definition of *"Substance abuse"* which *"*means the use, sale, or possession of illegal drugs, or the abuse of prescription and over-the-counter drugs, or the abuse of alcohol." Misuse is not specifically defined, but it is described in the SOC and 10 CFR Part 26 as being a policy violation if it amounts to substance abuse. The SOC provides examples of misuse, making it clear that there is a clear distinction between misuse and abuse:

> Misuse of prescription and over-the-counter medications may include, for example, the use of a spouse's or other family member's prescription medications that may cause impairment, such as some pain relievers, or the excessive use of some over-the-counter cold and cough preparations containing alcohol or other active ingredients that may cause impairment. However, an individual who has a substance abuse problem may use the same substances. For example, an individual who has become addicted to opiates may use a spouse's or other family member's codeine tablets or other opiates that were prescribed for pain relief to assist the addicted individual in avoiding withdrawal symptoms (NRC 2008).

While misuse may result in impairment as well as trustworthiness and reliability concerns, it is not considered a policy violation but is reported. Any indication that misuse is attributable to a substance abuse disorder (based on clinical assessment revealing such abuse), is considered an FFD policy violation (§§ 26.75(e) and (f)). See Section 3.3 for a more in-depth look at responses to impairment and Table 3.1, specifically, for an overview of FFD policy sanctions for varying scenarios of prescription drug use, misuse, and abuse.

A review of the literature reveals noteworthy trends associated with prescription drug misuse and abuse. According to NIDA (2018) prescription drug misuse, "has increased in the past fifteen years." Medications most commonly misused include CNS depressants, opioids, and stimulants, all of which are classes of medications identified as controlled substances under the CSA (Schedules II-IV), and are more likely to be misused in part because of their potential for psychological or physiological dependence, and are therefore also correlated with an increased chance of users developing a substance abuse disorder (SAMHSA 2017). Results from a 2015 National Survey on Drug Use and Health revealed that most people who misuse a DEA-scheduled prescription drug are not doing so for the purpose of getting high but to achieve the desired effect for which the prescription drug was prescribed, such as to treat pain (i.e., opioids), stay awake (i.e., stimulants), or relax (i.e., tranquilizers) (SAMHSA 2017). Such misuse can result in dependence, overdoses, and death. This type of misuse and abuse is a growing concern among older adults because they have increased medication sensitivity, slower metabolism, and may experience more impairment and increased chances of dependency at smaller doses (SAMHSA 2012).

In addition to widespread concern about misuse and abuse of DEA-controlled scheduled prescription drugs, the abuse potential of unscheduled medications is often overlooked (FDA 2019b and Traynor 2017). Gabapentin is an example of an unscheduled medication that is recognized by the medical community as a drug that has abuse potential. While not on the DEA schedules, many states have begun scheduling it on State-controlled schedules as trends in use, abuse, and overdose continue to rise (Buscaglia et al. 2019).

Table 2-2. High-level overview of drug misuse and abuse.

Agency/Researcher	Misuse	Abuse
NIDA	"… taking a medication in a manner or dose other than prescribed; taking someone else's prescription, even if for a legitimate medical complaint such as pain; or taking a medication to feel euphoria (i.e., to get high). The term *nonmedical use* of prescription drugs also refers to these categories of misuse" (NIDA 2018a).	According to NIDA (2018b), the term "misuse is roughly equivalent to the term abuse. Substance abuse is a diagnostic term that is increasingly avoided by professionals because it can be shaming and adds to the stigma that often keeps people from asking for help. Substance misuse suggests use that can cause harm to the user or their friends or family."
National Survey on Drug Use and Health (NSDUH)[(a)]	The use of prescription drugs in any way not directed by a doctor, including (1) use without a prescription; (2) use in greater amounts, more often, or longer than individual was told to take them; or (3) use in any other way a doctor did not direct the individual to use them (SAMHSA 2016, 2017)[(b)]	Substance use disorder as the result of misuse of a prescribed psychotherapeutic drug (SAMHSA 2019a)
SAMHSA (2012) citing Diagnostic and Statistical Manual (DSM)-IV (APA 2000)	"Dose level more than prescribed, longer duration than prescribed, use for purposes other than prescribed, use in conjunction with other medications or alcohol, skipping doses/hoarding drug" (SAMHSA 2012, citing APA 2000)	"Use resulting in declining physical or social function, use in risky situations (hazardous use), continued use despite adverse social or personal consequences" (SAMHSA 2012, citing APA 2000)
U. S. Food and Drug Administration (Smith et al. 2013) citing "Guidance for Industry Assessment of Abuse Potential of Drugs" (FDA 2010)	"The use of a drug outside label directions or in a way other than prescribed or directed by a healthcare practitioner. This definition includes patients using a drug for a different condition than that for which the drug is prescribed, patients taking more drug than prescribed or at different dosing intervals, and individuals using a drug not prescribed for them although for therapeutic purposes." (Smith et al. 2013:17, citing FDA 2010).	"The nonmedical use of a drug, repeatedly or even sporadically, for the positive psychoactive effects it produces" (Smith et. al 2013:18, citing FDA 2010)
Smith et al. 2013[(c)]	"Any intentional therapeutic use of a drug product in an inappropriate way. Misuse specifically excludes those events that meet the definition of abuse." Inappropriate use may include "use of a drug in a manner other than prescribed, directed by a healthcare provider, or presented in information provided to the patient." (Smith et al. 2013:7)	"Any intentional, non-therapeutic use of a drug product or substance, even once, for the purpose of achieving a desirable psychological or physiological effect" (Smith et al. 2013:7)

(a) NSDUH is directed by SAMHSA to conduct surveys of drug, alcohol, and tobacco use. NSDUH collects information about the reasons people misuse prescription psychotherapeutic drugs, focusing on pain relievers, tranquilizers, stimulants, and sedatives. Survey results are reported annually (NSDUH 2020 |https://nsduhweb.rti.org/respweb/homepage.cfm|).

(b) In prior surveys, NSDUH used the term "nonmedical use," which was defined "as use of prescription drugs that were not prescribed for an individual or were taken only for the experience or feeling that the drugs caused" (SAMHSA 2016). NSDUH revised the terminology to address shortcomings associated with the adequacy of the definition to accurately capture reports of legitimate use based on the intended effects of the drug, use of medication prescribed for someone else but for its intended effects (i.e., use of an opioid for pain relief, or a stimulant to stay awake), or overuse of a medication.

(c) This paper is authored by multiple members of the medical community who are focused on developing consistent terms for the purposes of clinical trials.

2.4.4 Impairment

Despite extensive information about medications, accurately predicting whether drug effects will impair an individual is often difficult, and individuals frequently do not recognize their own prescriptions as being potentially impairing (Pollini et al. 2017; Rudisell et al. 2016). Further, a significant portion of the population is medicated but goes about their daily routine with apparently little to no recognition of their increased risk for accidents (GAO 2015; NCHS 2017a; FDA 2018b). Thus, concerns about prescription drug use in the workplace are well-warranted, particularly for drugs that affect mood, cognition, sleep, physical abilities, or reaction times (Zezima and Goodnaugh 2010; Dumbacher and Evans 2018; MacDonald 2017).

The potential for human performance impairment from drug effects is long established, but studies that correlate workplace impairment with drug impairment tend to focus on substance abuse and/or cases resulting in injury (Ramchand et al. 2009). Other studies of drug effects and their effects on human performance are available and provide insights into possible workplace impairment (Stein and Strickland 1998; Ramchand et al. 2009). Before the mid-1990s, there were few studies of the potential cognitive effects of medications (Stein and Strickland 1998). The early review (by Stein and Strickland) of such impairment found many neuropsychological effects associated with antidepressants, anxiolytics, stimulants, antihypertensives, antiepileptics, and antihistamines (a set of drug classes selected to be representative for commonly used medications). The review found the drugs' sedative and anticholinergic properties to be central to producing neuropsychological impairments. The authors also expressed concerns about polydrug use and noted that tolerance may be a factor in some drugs' observed effects. They cautioned that,

> … effects co-occur or interact with a multitude of patient, treatment, and biochemical factors, such as the presence of psychological and neurological disorders, age, ethnicity, sociocultural, metabolic capacity, liver and kidney functioning, sedation, plasma drug levels, chronicity of treatment, tolerance, and interactions with other medications.

The UK Biobank large cohort study has functional performance data correlated with medication information in a database of more than 500,000 people (FDA 2018b).[19] A recent study investigated these data for drug effects on cognitive function and found that most drugs (262 of 368) were not associated with cognitive effects (Nevado-Holgado et al. 2016).[20] Medications highlighted in the study as having a significant cognitive performance effect are outlined in Table 2-3. The authors noted that their findings should be used with caution because of the study limitations, and that association between a medication and poor performance may reflect an underlying disease rather than a drug effect.

[19] The UK Biobank is a population-based cross-sectional cohort study that includes data about verbal–numerical reasoning (n = 165,493), memory (n = 482,766), and reaction time (n = 496,813) along with the individuals' health and medication data. These data are available as a major health information resource with the aim of improving the prevention, diagnosis, and treatment of a wide range of serious and life-threatening illnesses. The UK Biobank data set is based on data collected from the more than 500,000 people who were between 40–69 years old in 2006–2010 from across the United Kingdom. See https://www.ukbiobank.ac.uk/about-biobank-uk/ for more information.

[20] The Nevado-Helgado study controlled for age, gender, education, household income, smoking, alcohol status, psychostimulant/nootropic medication use, test center, and concurrent diagnoses and medications, and only evaluated medications that had a statistically significant number of users in the cohort.

Table 2-3. Summary of cognition effects from Nevado-Helgado et al. (2016).

Drug Category	Increased Cognitive Performance (Reasoning/Memory)	Decreased Cognitive Performance (Reasoning/Memory)	Faster Reaction Time	Slower Reaction Time
Nervous system disorder		Levetiracetam, Topiramate		Benzamides, Primidone, Risperidone
Cardiovascular	ACE inhibitors (e.g., perindopril)	Calcium channel blockers (e.g., amlodipine), diuretics (e.g., furosemide)		
GI tract and metabolism system		Proton pump inhibitors (e.g., omeprazole), diabetes (insulin)		Proton pump inhibitors (e.g., omeprazole), insulin, laxatives (contact and osmotic)
Immunomodulating[(a)]	Ibuprofen		Ibuprofen	

ACE = Angiotensin converting enzyme
(a) A slight, but not significant, association with better cognitive performance was seen for other anti-inflammatory medications.

The concerns about drug-impaired driving have engendered much research into the role that prescription drug impairment has on safe driving (GAO 2015). Literature reviews from multiple studies of drug-impaired driving provide an overview of the current understanding, including insights into possible workplace impairment because driving is a relatively complex task relying on both cognition and physical response. The National Highway Traffic Safety Administration (NHTSA) states that, “Many substances can impair driving, including alcohol, some over-the-counter and prescription drugs, and illegal drugs.” The difficulties in establishing controls for drug effect impairment are reflected in the fact that drugged driving laws have been enacted in only 22 states (NHTSA n.d.-a; GHSA n.d.).

A review investigating the role of drug use on motor vehicle collisions noted, “Several medications were associated with an increased risk of MVC [motor vehicle collision] and decreased driving ability” (Rudisell et al. 2016).[21] This analysis covered the 53 drugs evaluated in the reviewed studies; a summary of their findings for individual medications is presented in Table 2-4. The authors noted, “… certain medications, even within the same class or drug category, may be more associated with crash risk than others.” This review also noted that the association between a specific medication and risk of motor vehicle collision and driving ability is not always clear. Specifically, based on the evidence from motor vehicle crashes as well as driving performance data, some medications were associated with an increased incidence of motor vehicle collision but indicated no observed decrease in driving ability.

[21] From 6,516 sources initially identified as being pertinent for the Rudisell review, this study selected 27 sources for review that met the study’s inclusion criteria: studies published from English-language sources after 1959, licensed drivers 15 years of age and older, peer-reviewed publications, master’s theses, doctoral dissertations, conference papers, studies limited to randomized control trials, cohort studies, case-control studies or case-control type studies outcome measure reported for at least one specific medication, and outcome measures reported as the odds or risk of a motor vehicle collision (Rudisell et al. 2016).

Table 2-4. Summary of driving impairment findings from Rudisell et al. (2016).

Drug Category	Associated with Increased Incidence of Motor Vehicle Crash	Mixed Results on Association with Increased Incidence of Motor Vehicle Crash	Not Associated with Increased Incidence or Trending Toward Being Protective for Motor Vehicle Crash
Analgesics	Buprenorphine, Dihydrocodeine, Methadone	Codeine, Tramadol	Aspirin, Morphine
Anticonvulsants			Carbamazepine, Phenytoin, Valproate
Antidepressants		Trazodone	Amitriptyline, Dosulepin, Fluoxetine, Mirtazapine, Paroxetine, Sertraline, Venlafaxine
Antihistamines		Levocetirizine	Astemizole, Brompheniramine, Chlorphenamine, Desloratadine, Fexofenadine, Hydroxyzine, Levocetirizine, Loratadine, Terfenadine
Antihyperglycemics		Insulin	Metformin, Sulfonylurea[(a)]
Benzodiazepines	Flunitrazepam, Flurazepam, Lorazepam, Temazepam, Triazolam	Diazepam, Nitrazepam	Chlordiazepoxide, Oxazepam
Sleep medications	Zolpidem, Zopiclone		
Other medications	Carisoprodol (muscle relaxant)	Lithium (antipsychotic)	Atenolol (beta-blocker), Estrogen (hormone), Methyldopa (antihypertensive), Propranolol (beta-blocker), Salbutamol (antispasmodic), Warfarin[(b)](anticoagulant)

(a) Sulfonylurea was found protective against motor vehicle crash.
(b) Warfarin was found protective for new users but after time had no association.

The European Union's extensive research project on Driving Under the Influence of Drugs, Alcohol and Medicines, known as the DRUID project, looked at experimental studies, epidemiological studies, enforcement, classification of medicines, driver rehabilitation, withdrawal of driving license, and dissemination and guidelines related to road safety policy (Schulze et al. 2012).[22] A summary review of the DRUID project focused on understanding the scope of the drugged driving problem and identifying a range of appropriate countermeasures (Schulze et al. 2012). Salient findings from this study included the following:

[22] The DRUID project was a large research effort carried out in the European Union between 2006 and 2011 to investigate driving under the influence of drugs, alcohol, and medicines. The project ran for 5 years and involved 38 consortium partners from 17 Member States and Norway. The project evaluated epidemiological data for a standardized set of over 20 substances (including alcohol) generated from saliva and blood samples collected roadside (from more than 50,000 drivers) and at hospitals (from 2,492 drivers seriously injured and 1,118 driver fatalities) (Schulze et al. 2012).

- Alcohol remains one of the most dangerous psychoactive substances used by drivers.
- There are medicines that can cause impairment of which the patient is unaware.
- Drug packaging should be modified to indicate the degree of drug impairment.
- For drugged driving, a legal limit for patients undergoing long-term treatment is inappropriate and sanctions should be based on the degree of impairment.

The DRUID project ranked drugs by category and dose for impairment duration and maximum effect; these findings are presented in Table 2-5 (Schulze et al. 2012). Notably, drugs in the same category can range from no effect to a potentially large degree of impairment. Further, for drugs that cause impairment, the impairment tends to increase with increased dosage.

Table 2-5. Summary of driving impairment findings from the DRUID project (Schulze et al. 2012)

Drug Category	Substance/Dose (mg)	Degree of impairment[(a)]	Drug Category	Substance/Dose (mg)	Degree of impairment[(a)]
Anxiolytics	Buspirone (10)	0	Hypnotics and sedatives	Temazepam (10)	0
	Buspirone (20)	0		Zolpidem (5)	0
	Clobazam (10)	0		Lormetazepam (1)	22
	Clobazam (20)	0		Temazepam (20)	40
	Meprobamate (400)	0		Zaleplon (10)	40
	Meprobamate (800)	0		Triazolam (0.25)	89
	Diazepam (5)	17		Flunitrazepam (1)	115
	Diazepam (10)	57		Zolpidem (10)	119
	Lorazepam (1)	64		Zolpidem (20)	214
	Oxazepam (15)	104		Zopiclone (7.5)	240
	Diazepam (15)	112		Triazolam (0.5)	247
	Oxazepam (30)	170		Flunitrazepam (2)	461
	Diazepam (20)	171	Antidepressants	Fluoxetine (60)	0
	Alprazolam (1)	369		Paroxetine (30)	0
	Lorazepam (2)	418		Imipramine (75)	32
	Lorazepam (2.5)	571		Trazodone (100)	87
Antihistamines	Fexofenadine	0		Mianserin (10)	185
	Loratadine (10)	0		Amitriptyline (25)	327
	Terfenadine (60)	0		Amitriptyline (50)	380
	Diphenhydramine (25)	54	Antipsychotics	Sulpiride (400)	0
	Diphenhydramine (50)	92		Haloperidol (3)	93
				Promethazine (27)	491

(a) Degree of impairment is based on the integration of the greatest degree and duration of drug effect.

In sum, for most drugs, there are limited standards and understanding on which to base decisions related to prescription drug use and workplace impairment. Some drugs have been found to have generally unacceptable effects, but even these effects may be small or not manifest at lower doses and the impairment may be due to the underlying condition. Very few drugs have been found to be performance enhancing. For most drugs, the consensus about impairment acceptability appears to be that context is key; that is, the drug's effects on an individual and the activity being performed should be evaluated together to establish whether the effect is impairing.

2.4.5 Prescription Drug Monitoring Programs

Prescription Drug Monitoring Programs (PDMPs also sometimes called PMPs) are electronic drug registries that track and provide information about controlled substances and additional drugs of concern. PDMPs collect prescribing and dispensing information provided by pharmacies and dispensing practitioners. PDMP information can aid healthcare professionals, public health officials, public safety agencies, regulatory boards, and others in providing patient care and community health oversight. Although PDMPs are often touted as being critical to efforts made to stem opioid abuse, they also track the use of other controlled substances.

PDMPs have a long history— the first two were established in New York in 1918 and in California in 1939; another 15 PDMPs were established by 2000 (FSMB 2018). Although the earliest PDMPs began with paper-based systems tracking limited substances, all of them currently use electronic tracking tools and track the use of a significant portion of the controlled substances (FSMB 2018). Since 2000, the increasing number of opioid overdose fatalities has motivated establishment of new and overhaul of existing PDMPs; 53 PDMPs have been established by U.S. state, commonwealth, district, or territory governments.[23] Against this backdrop, efforts continue to modernize and integrate the myriad PDMPs as one of the tools available for fighting substance use disorders.

Because PDMPs were established independently, the details of their administration, drugs monitored, and reporting vary. Within the United States, PDMPs are operated by diverse types of agencies (see Table 2-6) (ASTHO 2017; PDMP TTAC 2019). All programs but Missouri's cover the entire jurisdiction.

Table 2-6. PDMPs are operated by diverse types of agencies.

Agency Type	Number	Jurisdiction (State)
Pharmacy Boards	20	AK, AZ, CO, IA, ID, KS, LA, MN, MS, MT, ND, NH, NM, NV, OH, SD, TN, TX, WV, WY
Department of Health	18	AL, AR, DC, FL, GA, KY, IL, OR, MA, MO, NE, NY, PA, RI, SC, VT, WA
Law Enforcement	4	CA, HI, NJ, OK
Professional Licensing Agency	6	DE, IN, MI, UT, VA, WI
Substance Abuse Agency	4	MD, ME, NC, PR
Consumer Protection Agency	1	CT

PDMPs typically monitor the controlled substances listed in DEA Schedules II–IV or II–V (see Section 2.3.3). None of the PDMPs include Schedule I drugs because they have no currently accepted medical use. A little over half of the PDMPs monitor additional drugs of concern that may cause addiction or be subject to diversion. These include both drugs that are controlled substances (e.g., butalbital products or chlordiazepoxide and combinations) and drugs of

[23] Missouri's State Government has historically resisted establishing a PDMP. Missouri's St. Louis County has independently established and operated a PDMP that incorporates participating jurisdictions (see https://www.stlouisco.com/healthandwellness/pdmp). The Governor established a PDMP by Executive Order in Missouri (Executive Order 17-18) (https://www.sos.mo.gov/library/reference/orders/2017/eo18).

concern that are not controlled substances, such as cyclobenzaprine or nalbuphine.[24] Table 2-7 provides an overview of the drugs monitored by each PDMP (PDMP TTAC 2018).

Table 2-7. Drugs monitored by PDMPs.

Drugs Monitored	Number	Jurisdiction (State)
Schedules II-V	13	AZ, CO, FL, GA, MD, MI, MT, NC, NM, PA, PR, SD, TX
Schedules II-V and drugs of concern	28	AL, AR, CT, DC, DE, ID, GU, HI, IL, IN, KY, LA, MA, MN, MS, ND, NE, NJ, NY, OH, OK, TN, UT, VA, WA, WI, WV, WY
Schedules II-IV	10	AK, CA, IA, NV, ME, MO, NH, SC, VT, RI,
Schedules II-IV and drugs of concern	2	OR, KS

Each PDMP is independent and maintains its own database, but most PDMP registries are coordinated in the PDMP national network run by the National Association of Boards of Pharmacy.[25] The PDMP network enables data exchange between participating PDMPs. All PDMPs have common requirements for data protection and dissemination, which, according to the National Alliance for Model State Drug Laws, include the following:

- Provide data upon request to authorized entities at any time via secure websites.
- Collect information about dispensed controlled substance prescription drugs.
- Use the data format developed by the American Society for Automation in Pharmacy.
- Use HIPAA-compliant security systems to protect sensitive information.
- Protect patient confidentiality.
- Each PDMP's governing statutes, regulations, and orders provide for authorized user access to PDMP data; this access varies between programs. Authorized users typically include a selection of individuals and organizations from the following categories:
  - Medical professionals – Physician assistant, nurse practitioner, prescriber delegate, medical resident, intern (typically requires a physician-patient relationship, thus excludes Medical Review Officers [MROs] except where an individual has granted permission for consultation with his or her medical professional)[26]
  - Dispensing professionals – pharmacists, pharmacies, dispenser delegate, marijuana dispensary
  - Law enforcement – Medicaid fraud and abuse, Medicaid drug utilization and review, drug court, medical examiner/coroner

[24] Cyclobenzaprine is a muscle relaxant that may be used non-medically to induce euphoria or relaxation (https://www.deadiversion.usdoj.gov/drug_chem_info/cyclobenzaprine.pdf). Nalbuphine is a synthetic narcotic analgesic (https://www.deadiversion.usdoj.gov/drug_chem_info/cyclobenzaprine.pdf).

[25] As of November 2018, the National Association of Boards of Pharmacy PMP InterConnect® had more than 45 active and pending participants. See https://nabp.pharmacy/initiatives/pmp-interconnect/ for more information.

[26] Medical professional access to a PDMP typically requires a physician-patient relationship, thus excluding MROs. See, for example, https://www.lsbme.la.gov/sites/default/files/documents/Advisory%20Opinions/Medical%20Review%20Officer.pdf

- Legal professionals – Prosecutor, Medicaid fraud and abuse, drug court, correctional supervision
- Licensing and regulatory boards – Health department, pharmacy board, law enforcement, and other government or professional agencies
- Other – other PDMP, researcher, patient.

Provisions for reporting and conducting database checks vary, in some cases considerably, between PDMPs. For example, prescribers and dispensers are required to provide required information to the PDMP within the required timeline, which ranges between PDMPs from daily up to weekly (NAMSDL 2018a). Additional processing time may be required for these data to be loaded into the PDMP database (FSMB 2018). In 37 jurisdictions, prescribers must check the PDMP database prior to initiating new opioid prescriptions (NAMSDL 2018b). This check may be done by a delegate in some jurisdictions, while in others it must be done by the prescriber.

PDMP use is climbing and has the advocacy of the American Medical Association and the CDC as a tool in the fight against opioid abuse (CDC 2019; CDC n.d.). PDMPs are evolving, largely in response to the opioid crisis, and with possible structural improvements including enhanced interconnectivity, more timely information availability, more comprehensive information, and better integration with electronic health records (CDC 2018b). There are drawbacks, however, given the extensive amount of personal health information in these databases. Controls on law enforcement use varies and criminal actions have been pursued against individuals that in some cases turned out to be unfounded (Schwartzapfel 2017). According to the CDC,

> Prescription drug monitoring programs (PDMPs) continue to be among the most promising state-level interventions to improve opioid prescribing, inform clinical practice, and protect patients at risk. Although findings are mixed, evaluations of PDMPs have illustrated changes in prescribing behaviors, use of multiple providers by patients, and decreased substance abuse treatment admissions (CDC 2017).

3.0 FFD and Prescription Drug Use

Maintaining a workforce that is fit for duty requires licensees to manage for possible impairment of individuals from legal use of prescription drugs. To do this successfully, the FFD program must accommodate the wide variety of drugs that may be prescribed,[27] while accounting for the actual effects experienced by the individual. The FFD program addresses this by ensuring each individual's fitness for duty is considered with respect to job duties and drug effects on a case-by-case basis.

The NRC has broad, coordinated provisions for fitness for duty and access authorization that apply to both licensees[28] and covered individuals. FFD program effectiveness relies upon the licensee's implementation and management of requirements and the covered individuals' cooperation with and adherence to the requirements. Each licensee's FFD program is established through licensee-specific policy, procedures, and training.

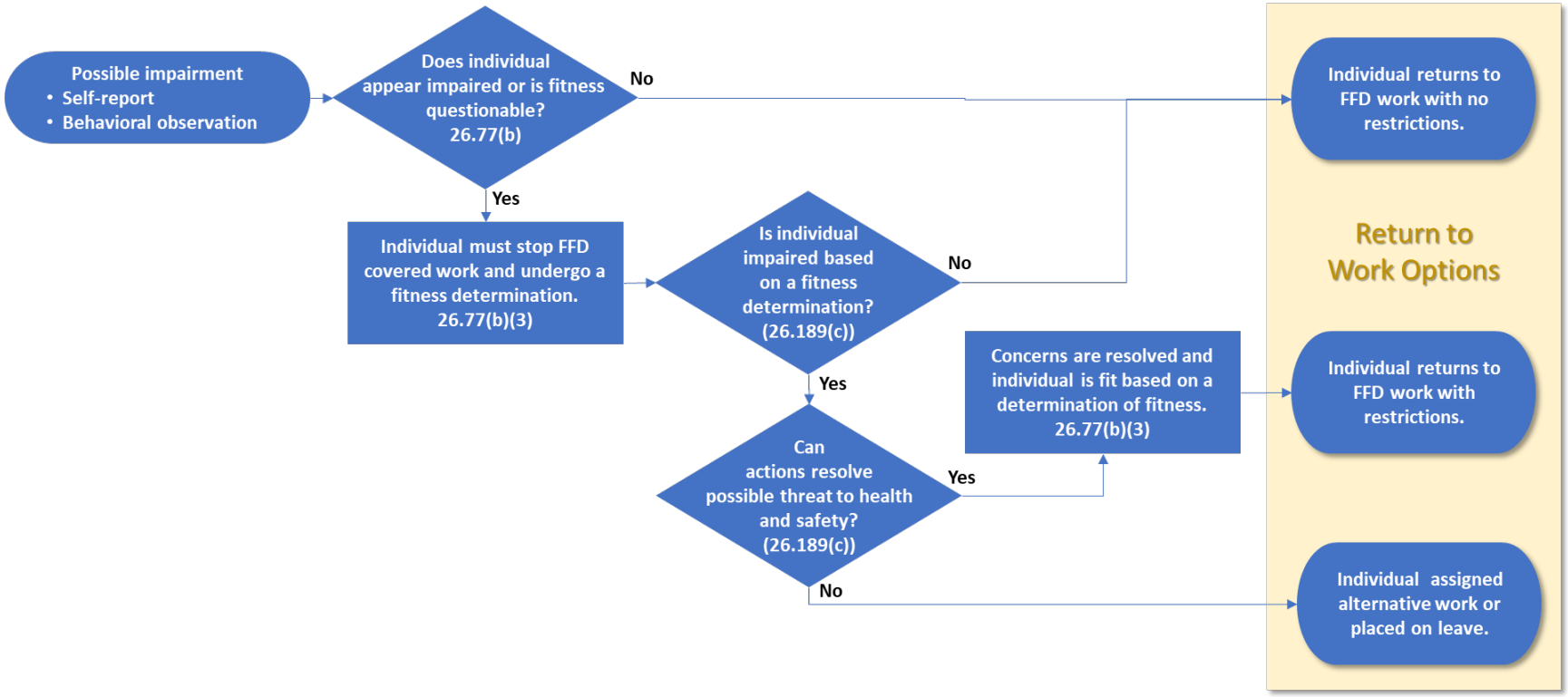
The FFD program is grounded in the performance objectives at 10 CFR 26.23 that, in part, require licensees have reasonable assurance of the following:

- Individuals are trustworthy and reliable as demonstrated by the **avoidance of substance abuse**.
- Individuals are **not under the influence** of any substance, legal or illegal, **or mentally or physically impaired** from any cause, which in any way adversely affects their ability to safely and competently perform their duties.
- There are reasonable measures for the **early detection** of individuals who are not fit to perform the duties that require them to be subject to the FFD program.

From the individual's perspective, the key day-to-day FFD program activities for meeting the performance objectives are self-reporting, behavioral observation, and, if needed, fitness determination. These three activities shape the process a licensee must follow for ensuring that a potentially impaired individual does not present a threat to workplace or public health and safety (see Figure 3-1). Individuals identified as being possibly impaired and potentially incapable of safely and competently performing their job duties require a determination of fitness. If found fit for duty, the individual may return to work. If found not fit for duty, the individual may return to work only when the impairing or questionable conditions are resolved, and a determination of fitness indicates that the individual is fit to safely and competently perform his or her duties. If a determination of fitness is not possible, and the individual's condition cannot be resolved, then the individual cannot return to those duties.

[27] There were more than 5,000 unique, non-proprietary registered drugs on the FDA's National Drug Code Directory on August 14, 2019.
[28] For the purposes of this report, the term licensee includes licensees and other entities subject to the FFD programs per 10 CFR 26.3.

Figure 3-1. Process for resolving concerns about a potentially impaired individual.



3.1 General FFD Program Requirements

The licensee's FFD policy, procedures, and training establish the framework for each licensee's implementation and management of the FFD program. These are among the required FFD program elements listed in 10 CFR Part 26 Subpart B (§§ 26.21 – 26.41). The absence of well-crafted FFD policy, procedures, and training could lead to inconsistent program implementation and over- or under-reporting of FFD concerns that may lead to licensee vulnerability for violation of FFD requirements or other employment law (see Section 5.0).

Licensees are required to have a policy statement that is available to all individuals who are subject to the policy (§ 26.27(b)). In general, the policy statement must have sufficient detail to inform affected individuals of what is expected of them and what consequences may result from not adhering to the policy. Other parts of the required licensee policy relevant to prescription drug use are as follows:

- description of the consequences of the use, sale, or possession of illegal drugs on or off site; the abuse of legal drugs and alcohol; and the misuse of prescription and over-the-counter drugs;
- description of the requirements for reporting to the collection site for random testing within a specified time, what actions constitutes a refusal to test, and consequences for refusing to test or subverting or attempting to subvert the testing process;
- addressing other factors that could affect an individual's fitness for duty, including use of prescription and over-the-counter medications that could cause impairment;
- description of any program that is available to individuals who are seeking assistance in dealing with drug problems that could affect an individual's fitness for duty;
- description of the consequences of violating the policy;
- description of the individual's responsibility to report legal actions by a law enforcement authority or court of law including an arrest, an indictment, the filing of charges, a conviction, or mandated implementation of a substance abuse treatment related to use sale or possession of illegal drugs, abuse of legal drugs, or the refusal to take a drug test;
- description of the responsibilities of managers, supervisors, and escorts to report FFD concerns; and
- description of the individual's responsibility to report FFD concerns.

Licensees must also prepare and maintain written procedures that describe the methods for implementing the FFD policy and other FFD program requirements. In accordance with § 26.27(c), FFD program procedure topics relevant to prescription drug use include the following:

- Describing the process for ensuring that individuals who are called in to perform an unscheduled working tour are fit for duty. At a minimum the procedure must require the individual who is called in to state whether the individual considers himself or herself fit for duty.
- Describing the process to be followed if an individual's behavior raises a concern regarding impairment, which could adversely affect the individual's ability to safely and competently perform his or her duties.

- Requiring that individuals who have an FFD concern about another individual's behavior must contact the personnel designated in the procedures to report the concern.

Licensees must also ensure affected individuals have specific knowledge and abilities under the training requirements at § 26.29. These include several provisions relevant to legal prescription drug use, including knowledge about the following:

- policy and procedures that apply to the individual, the methods that will be used to implement them, and the consequences of violating the policy and procedures;
- the individual's role and responsibilities under the FFD program;
- the roles and responsibilities of others (e.g., the MRO and the Human Resources, FFD, and Employee Assistance Program [EAP] staff);
- EAP services that are available;
- personal and public health and safety hazards associated with abuse of legal drugs;
- potential for adverse effects on job performance due to prescription drugs;
- potential for prescription and over-the-counter drugs and dietary factors to affect drug and alcohol test results;
- recognizing illegal drugs and indications of the illegal use, sale, or possession of drugs;
- how to observe and detect performance degradation, indications of impairment, or behavioral changes;
- the individual's responsibility to report an FFD concern and their ability to initiate appropriate actions, including referrals to the EAP and person(s) designated by the licensee or other entity to receive FFD concerns.

The NRC's FFD program categorizes labor at § 26.4 by general duties: operators, emergency response staff, maintenance workers, security, and other covered individuals (see Appendix D for more detail). Within each of the defined job categories and for other covered individuals, actual job duties will vary and must be considered when evaluating whether a drug effect is impairing and whether there is an underlying condition of concern that necessitates considering whether reasonable controls or alternative duties may be appropriate.

3.2 Integration with Access Authorization Program Requirements

The FFD program underwent a significant modification in 2008 that included enhancing consistency with the NRC's access authorization (AA) requirements for nuclear power plants (NPPs) under § 55 and § 73.55 and § 73.56 (73 FR 16966).[29,30] Under the NPP AA program, NPP licensees must assure unescorted access is only granted to individuals who

[29] There are other access authorization regulations (e.g., § 73.38 and Part 37), but they are focused on trustworthiness and reliability and do not have equivalent provisions for medical issues and behavioral observations as those found in the NPP access authorization rules.

[30] The Nuclear Energy Institute (NEI) has developed and maintained the *Nuclear Power Plant Access Authorization Program* (NEI 03-01 [NEI 2014]), a document that provides standard industry criteria for implementing the Access Authorization Rule and establishes consistency in AA programs throughout the industry.

- are trustworthy and reliable,
- do not constitute an unreasonable risk to the health and safety of the public or the common defense and security, and
- do not pose a threat for interrupting the normal operations of the plant or committing radiological sabotage.

Under § 55.3, to perform the function of an NPP operator or senior operator, individuals must be authorized under an operator's or senior operator's license issued by the Commission. Among the requirements for this license, the individual must meet and the NPP licensee must certify that medical requirements are met for 10 CFR Part 55 Subparts C and D (§ 55.21 et seq. and § 55.31 et seq., respectively). These requirements include a medical examination of the individual by a physician every two years to ensure the individual's medical condition and general health will not adversely affect the performance of assigned operator job duties or cause operational errors that endanger public health and safety (§ 55.33(a)(1)). This information feeds into the Commission's determination about whether to issue an NPP operator's license for that individual. In cases in which an individual has a permanent condition and does not meet minimum standards, the NRC may approve a conditional license. Typical conditions for a conditional license include corrective lenses, hearing aids, no solo operation, take medication as prescribed, and no duties requiring a respirator. If an NPP operator has a permanent change in his or her physical or mental condition that causes the individual to fail to meet medical fitness requirements, the licensee must inform the NRC within 30 days (§ 55.25). For an NPP operator who has a temporary condition, the licensee may administratively limit that operator's duties.

In addition to maintaining and certifying a licensed nuclear operator's medical fitness, under § 73.55(b)(7), NPP licensees are required to establish, maintain, and implement an AA program in accordance with § 73.56. Under a § 73.56(f) AA program, individuals are subject to behavioral observation, behavioral observation training, and mandatory reporting for observed behavioral concerns. These behavioral observation requirements complement the FFD program requirements for behavioral observation at § 26.33 and 407.

With respect to prescription drug use, the behavioral observation and reporting requirements at § 73.56(f) for NPPs bolster FFD requirements for reporting and impairment. For the subset of the workers covered by both programs, FFD and AA rules provide a coordinated framework for managing the use of prescription drugs through granting, maintaining, and terminating individuals' authorization for unescorted access to a licensee's facility or material by assuring those individuals are trustworthy, reliable, and fit to perform their assigned duties (see Figure 3-2).

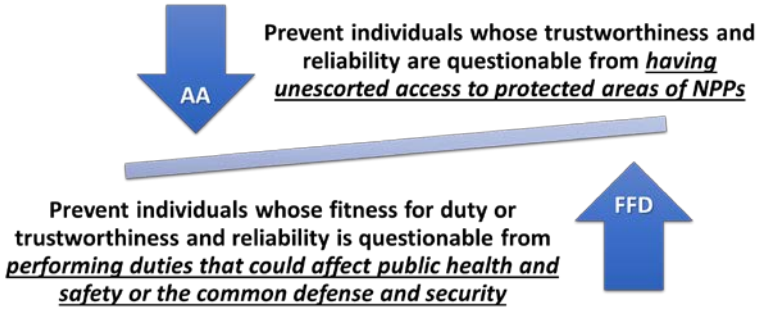


Figure 3-2. FFD and NPP AA regulations are complementary.

3.3 Response to Impairment

For legal use of prescription drugs, FFD program rules are not proscriptive, rather they are predicated upon evaluating individual response to medications with respect to assigned work duties.[31] This approach relies upon the affected individuals and their co-workers' ability to recognize impairment and trustworthiness to report potential impairment. FFD program provisions ensure that, in the absence of policy violation, the individual's condition and work duties are considered before the individual is deemed fit for duty, assigned alternative duties, or placed on leave. Further, as the individual's condition changes, new information is made available, or an accommodation is made, the individual's evaluation and recommendation are updated.

A critical component of understanding workplace impairment is determining whether a drug affects an individual's ability to perform assigned job duties. In addition, it may be necessary to determine if the underlying condition is impairing for the assigned job duties even in the absence of the prescribed medication. The NRC's FFD program categorizes labor at § 26.4 by general duties: operators, emergency response staff, maintenance workers, and security (see Appendix D for more detail and a list of other covered individuals). Within each of the defined job categories (and for other covered individuals), the actual job duties will vary. The job duties are used in determining whether a drug effect is impairing, whether there is an underlying condition of concern, and what reasonable controls or alternative duties may be appropriate.

3.3.1 Policy, Procedures, and Training

The licensee's framework for assuring that an individual's impairment is noticed and addressed is established in their written FFD policy and procedures. The policy and procedures must be available to all individuals, and the individuals must have enough training to learn and understand his or her role in implementation of FFD policy and procedures. Training is critical to the success of the FFD program's implementation—authorized individuals must understand the potential for impairment and be able to recognize and report cases where they or a coworker is potentially not fit for duty. This assures that if an individual does not realize his or her own impairment, co-workers and managers are trained to notice and report their possible impairment.

How the licensee's FFD policy addresses use of prescription drugs should be made clear to covered staff and consistently applied. The policy must be crafted and implemented to avoid creating a chilling environment—one in which individuals are reluctant to self-report prescription drug side effects or behavioral observation issues for others—as well as averting over-reporting to avoid work. Good practices for written policy about use of prescription drugs should include, but not be limited to, the following topics in addition to the requirements discussed in Section 3.1:

- duty to report possible impairment;
- definition of legal use, misuse, and abuse;

[31] How the rule defines and constrains illegal drug use informs the boundaries for acceptable prescription drug use under the FFD requirements. As defined at 10 CFR 26.5, "*Illegal drug* means, for the purposes of this regulation, any drug that is included in Schedules I to V of section 202 of the Controlled Substances Act [21 U.S.C. 812], but not when used pursuant to a valid prescription or when used as otherwise authorized by law."

- definition and signs of impairment;
- whether specific medications are allowed or excluded at the licensee facility or its areas;
- mechanisms for individuals to confidentially report possible impairment;
- mechanisms for reporting another individual exhibiting impaired behavior;
- a process for determining fitness, including roles and responsibilities of licensed professionals (e.g., substance abuse expert [SAE], MRO, or other professional) and the need for clear job duty definition for evaluating an individual's capabilities;
- processes for determining appropriate accommodation and what type of options are available when needed for temporary or permanent impairment (e.g., work assignment restrictions, placed on leave, etc.);
- process for returning to normal work duties;
- consequences for violating prescription drug-use policy; and
- required record-keeping.

Training is critical to the success of this approach—the workforce and their managers must understand the potential for impairment and be able to recognize and report cases in which an individual is potentially not fit for duty. Each individual must demonstrate successful completion of training prior to initial authorization and annually thereafter by passing a comprehensive test to maintain authorization (§ 26.29(b)). Refresher training must be completed in cases in which an individual fails to pass the annual test; fails to properly implement FFD program procedures; or if warranted by the frequency, nature, or severity of problems discovered through audits or the administration of the program. With respect to knowledge of and abilities to manage prescription drug use in the workplace, a covered individual's training should include, but not be limited to, the following:

- understanding individual job duties and what types of side effects may be impairing;
- understanding patient information about prescription drugs with respect to their side effects;
- understanding how to consult with physicians and pharmacists about drug side effects, including for interactions between multiple drugs, including over-the-counter medications and alcohol when considering new medications;
- recognizing impairment in one's self or others;
- understanding when and how to report impairment or potential impairment;
- understanding the determination of fitness process and when it is mandated;
- the potential outcomes in the event of impairment, including:
  - required licensed medical consult on drug regime
  - job restrictions
  - temporary leave
  - reassignment;
- the role of well-informed medical advice (e.g., personal physician/MRO/pharmacist) during the course of a potentially impairing drug regime.

Supervisors should have additional training, including

- handling sensitive individual medical information,
- compliance with ADA, Occupational Safety and Health Administration (OSHA), HIPAA, and Family and Medical Leave Act (FMLA).

3.3.2 Recognizing Possible Impairment

The FFD program relies on self-reporting and behavioral observation to recognize and report when an individual may be impaired due to prescription drugs and thus not fit for duty. This is a pragmatic approach that accommodates both the realities of medical care and the vagaries of individual response to medications. Policies and procedures for recognizing possible impairment must be crafted to assure FFD program consistency and understanding when a fitness determination is required. FFD program implementation should seek to minimize two potential issues. First, individuals may attempt to avoid work by self-reporting conditions that are not impairing or are exaggerated conditions with the expectation that he or she will be relieved from regular job duties. Second, impairment may be under-reported where licensee policies and procedures are punitive to those reporting possible impairment (i.e., a chilling environment). A fitness determination should be conducted whenever either a supervisor, a coworker, or the potentially impaired individual has reason to believe that an individual is not fit for duty.

When an individual is experiencing potentially impairing drug effects, he or she must self-report (§ 26.27(a)(11)). If an individual does not realize or report their own impairment, their co-workers and managers are trained to notice and report (§ 26.33). If an individual appears to be impaired or the individual's fitness is questionable, the FFD program requires that licensees must take immediate action to prevent the individual from performing covered work (§ 26.77(b)).[32] How well this process proceeds is dependent on the clarity and structure of the licensee's written policies and procedures, workforce training, and clear definition of job duties. In particular, assessment of an individual experiencing a drug effect will be best facilitated when clearly articulated job duties are available to compare with the individual's capabilities.

Once possible impairment is reported, it is possible that a first-line supervisor and an individual could discuss whether the individual can be assigned job duties that he or she can perform despite exhibiting a drug effect. If a supervisor or individual believes that the individual cannot safely perform assigned job duties, a fitness determination by a medical professional should be required.

Reliance on drug testing to detect impairment is not practicable—even when considering the most commonly prescribed medications, there are too many to test without significant cost burden among other challenges (see Section 3.4).[33] Further, although medications usually have known side effects, predicting whether these side effects will manifest in a particular individual is only certain in the cases where the drug or a metabolite affects a metabolic pathway (see Section 2.4.1).

[32] Except as permitted for individuals called in for unscheduled hours or with a waiver for fatigue (see §§ 26.27(c)(3), 26.207, and 26.209).
[33] The top 300 most commonly prescribed medications represent 97% of prescribed medications (see https://clincalc.com/DrugStats/About.aspx for more information).

3.3.3 Fitness Determination

A supervisor may permit a possibly impaired individual to return to work only after the impairing or questionable conditions are resolved and a determination of fitness indicates that the individual is fit to safely and competently perform their duties (§ 26.77(b)(3)). For individuals who are impaired because of legal use of prescription drugs and no other reason, the FFD program forbids sanctions (§ 26.189(c)(2)). For these individuals, because of other legal protections discussed in Section 5.0, licensees must determine in what capacity, if any, the affected individual may perform covered work.

The determination of fitness must be made in a face-to-face interaction by a licensed or certified professional who is appropriately qualified and has the necessary clinical expertise, as verified by the licensee or other entity. A professional called on by the licensee or other entity may not perform a determination of fitness regarding fitness issues that are outside of his or her specific areas of expertise. Qualified professionals for prescription drug impairment include, but are not limited to the following (§ 26.189(a)):[34]

- psychiatrists for psychoactive medications
- physicians for medications
- MROs for medications.

Whether an individual is impaired depends on the individual's response to their medication and whether his or her ability to perform specific job duties is compromised. Actual job duties will vary and are what must be considered when evaluating whether a drug effect or associated underlying condition of concern is impairing. Clearly articulated position requirements and job duty descriptions will facilitate determining whether an adverse side effect causes an individual to be incapable of performing his or her job functions. This is because the medical professional's fitness determination requires evaluating whether or not the specific fitness issues presented by the individual represent a threat to the workplace or public health and safety with respect to the individual's assigned job duties (§ 26.189(a) and (c)(2)). For the effects that may affect an individual's ability to perform under either normal or emergency conditions, conditional restrictions or alternative duties may be needed.

Selected examples of how side effects could affect an individual's ability to perform assigned job duties are listed below:

- Dizziness or lightheadedness may cause an individual to have balance issues and thus preclude some or all work at heights. If symptoms are mild, an individual may not be able to safely climb a ladder or use a lift platform but may be able to perform work on a balcony that does not require use of fall protection gear.
- Nausea or vomiting would preclude an individual from work requiring some types of personal protective equipment (PPE, e.g., face mask). Note that workers in some positions may only be required to wear PPE during emergency conditions yet must be ready to do so for the entire shift.

[34] Note that the MRO's defined responsibility in the FFD program is to review and interpret drug test results, identify any issues associated with collecting and testing specimens, and advise and assist in FFD program management in planning and overseeing the overall FFD program. For cases involving substance abuse, the FFD rules require the health professional to have training and expertise or certification to perform as an SAE.

- Muscle cramps or weakness could affect an individual's physical ability to respond immediately thus impairing physical capabilities. This type of impairment may be incompatible with positions requiring good physical capability such as security officers. Other workers, such as maintenance workers, may also be affected depending on job duties.
- Difficulty falling asleep or staying asleep is likely to lead to an individual being fatigued. Some medications may also cause drowsiness. While there are work hour restrictions for fatigue issues under the FFD program, fatigue as a side effect would be a different problem that would require other resolution. Depending on the severity of the condition, job duties may not be affected other than requiring the individual to have no solo work duties.

Appendix E lists 20 of the most popularly prescribed drugs and their associated side effects.

3.3.4 Response to Policy Violations

Whether prescription drug use in the workplace is a policy violation depends on the nature of drug use (e.g., legality of drug procurement and administration) and the legality of the drug being used. Prescription drug use is legal if the medication is legally prescribed by a healthcare professional such as a treating physician and is used in a manner as prescribed to serve therapeutic purposes. As mentioned in Section 1.0 and discussed in Section 5.5, prescription drugs or controlled substances obtained without a valid prescription or through fraud, deceit, or misrepresentation is unlawful. Taking unlawfully obtained drugs, if detected, might constitute a policy violation. In the FFD context, an illegal drug is "any drug that is included in Schedules I to V of CSA Section 202 (21 U.S.C. 812), but not when used pursuant to a valid prescription or when used as otherwise authorized by law" (Branch and Baker 2013). In particular, the use of Schedule I controlled substances is illicit because they have a high potential for abuse by users and no currently accepted medical use (DEA n.d.-a). Therefore, Schedule I controlled substances cannot be legally prescribed, dispensed, or administered for medical purposes.

10 CFR Part 26 specifies sanctions for individuals violating the FFD rule. For workplace prescription medication use, a number of scenarios need to be taken into consideration to address two central questions: (1) what constitutes policy violations in the context of fitness for duty regarding prescription drug use, and (2) what are the appropriate responses to policy violations in accordance with Part 26? In Table 3-1, we consider possible scenarios concerning prescription drug use in the workplace to shed light on these two questions.

In case of an FFD policy violation, sanctions will be imposed on individuals in accordance with § 26.75. Licensees and other entities are not precluded from imposing more severe sanctions than what is specified in the rule. The sale, use, or possession of illegal drugs shall result in immediate unfavorable termination of access authorization and authorization denial of a minimum of 5 years thereafter. 10 CFR Part 26 also mandates management actions concerning possible impairment on the job from substance abuse (10 CFR 26.77). If an individual appears to be impaired on the job, the licensee must immediately prevent the individual from performing duties that subject the individual to 10 CFR 26 Subpart D.

Table 3-1. Scenarios involving prescription drug use and policy violation.

Scenarios	Possible Mechanisms of Impairment Detection	FFD Policy Violation?	Sanctions
Impaired due to medical condition	• Behavioral observation • OSHA reporting in case of reportable incidents	No, because the individual did not take any illegal substances and did not take any prescription medication.	None based on Part 26. A fitness determination must be made to ensure the individual can safely and competently perform his/her duties (§ 26.189).
Impaired due to medical condition but intentionally taking no OTC or prescription medication to avoid self-reporting or taking sick leave	• Behavioral observation • OSHA reporting in case of reportable incidents	No, because the individual did not take any illegal substances and did not take any prescription medication.	None based on Part 26. Licensees or other entities might impose sanctions in their FFD programs.
Impaired while taking medication with a valid prescription for intended medical use at the dosage and frequency as prescribed.	• Self-reporting • Behavioral observation • OSHA reporting in case of reportable incidents • Drug testing if the drug is on the testing panel	No, because the individual did not take illegal substances and drug was administered as prescribed.	None based on Part 26. Licensees or other entities might impose sanctions or have sanctions in their FFD programs.
Impaired while taking prescription medication without a valid prescription (e.g., taking one's spouse's prescription medication) to treat a medical condition.	• Self-reporting impairment • Behavioral observation • Drug testing if the drug is on the testing panel • OSHA reporting in case of reportable incidents	Assumption: the drug is on the licensee's testing panel. Violation depends on whether clinical evidence of drug abuse is found. • Not a policy violation if the MRO determines that the donor has used another individual's prescription medication and no clinical evidence of drug abuse is found; the MRO shall report to the licensee or other entity the donor has misused a prescription medication (§ 26.185(j)(3)). • A policy violation if the MRO determines that the donor has used another individual's prescription medication and clinical evidence of drug abuse is found; the MRO shall report to the licensee that the donor has violated the FFD policy (§ 26.185(j)(3)).	In cases of misuse, the FFD rule stipulates that "sanctions for misuse of prescription and OTC drugs must be sufficient to deter misuse of those substances" (§ 26.75(f)). Specific sanctions might be specified in the FFD policy of the licensee or other entity. In cases of a policy violation, the sanctions are specified in § 26.75(e)(1)(2) & (g).

Scenarios	Possible Mechanisms of Impairment Detection	FFD Policy Violation?	Sanctions
Impaired while taking medication with a valid prescription at a dosage greater than prescribed.	• Drug testing if the drug is on the testing panel • Self-reporting • Behavioral observation • OSHA reporting in case of reportable incidents	Assumption: the drug is on the licensee's testing panel. Violation depends on whether clinical evidence of drug abuse is found. • No violation if the MRO determines that there is a legitimate medical explanation for a positive confirmatory drug test, and that use of a drug identified through testing was in the manner and at the dosage prescribed and the results do not reflect of lack of reliability or trustworthiness (§ 26.185 j(1)(2) and (k)). • Policy violation if the MRO determines that there is no legitimate medical explanation for a positive confirmatory test result for non-opiate prescription drugs; the MRO shall determine whether there is clinical evidence of abuse of any of these substances or their derivatives (§ 26.185(j)(1)(2)) and report the result as an FFD policy violation if evidence of drug abuse is found. • Policy violation if the MRO determines that there is no legitimate medical explanation for a positive confirmatory test result for opiates and the donor has illegally used opium, an opiate, or an opium derivative; the MRO shall report the test result as an FFD policy violation (§ 26.185(j)(1)).	In cases of misuse, the FFD rule stipulates that "sanctions for misuse of prescription and OTC drugs must be sufficient to deter misuse of those substances" (§ 26.75(f)). Specific sanctions might be specified in the FFD policy of the licensee or other entity. In cases of a policy violation, the sanctions are specified in § 26.75(e)(1)(2) & (g).
Impaired from using Schedule 1 controlled substances	• Drug testing • Behavioral observation • OSHA reporting in case of reportable incidents	Policy violation. The MRO may not consider the use of any drug contained in Schedule I of CSA Section 202 (21 U.S.C. 812) as a legitimate medical explanation for a positive confirmatory drug test result, even if the drug may be legally prescribed and used under State law (§ 26.185(j)(6)).	In case of a policy violation, the sanctions are specified in § 26.75(e)(1)(2) & (g).

FFD = fitness for duty; MRO = medical review officer; OSHA = Occupational Safety and Health Administration; OTC = over-the-counter.

Under Part 26, licensees and other entities are required to give notice to the individuals and inform the individuals of the basis on which the policy violation is determined. They are also required to give individuals charged with an FFD policy violation opportunities to respond to and provide additional pertinent information about the policy violation (10 CFR 26.39). If the review findings indicate such individuals did not violate the FFD policy, the favorable outcome should be recorded by the licensee or other entity and the information regarding the policy violation should deleted or corrected accordingly.

3.4 Prescription Drug Tests

FFD drug testing is designed to discover illegal use of specific drugs and is not intended for testing to reveal legal prescription drug use (§ 26.31(a)). The sheer number of prescription drugs that have potentially impairing effects, compounded by the fact that FFD rules only allow testing for DEA-scheduled drugs, makes drug testing an inappropriate tool for managing legal prescription drug use (§ 26.31(d)(1)(i)(A)).

All individuals must comply with the FFD program's testing requirements to gain and maintain authorization (Subpart C—Granting and Maintaining Authorization, § 26.51 et seq.). Testing is required for specific conditions (§ 26.31(c)).

Initial authorization and authorization updates require pre-access drug testing during the 30 days prior to granting authorization with limited exceptions. To maintain authorization, all individuals must be in a random testing program. Individuals may also be tested for possible substance abuse based on behavior, physical condition, or after receiving credible information that an individual is engaging in substance abuse. Finally, post-event drug testing is required in cases where human error may have caused or contributed to the event.

3.4.1 Drug-Testing Panel

A minimum required set of drugs must be included in the drug-testing panel and additional drugs may be added if specific conditions are met. The minimum required list of substances that must be tested for is marijuana metabolite, cocaine metabolite, opiates (codeine, morphine, 6-acetylmorphine), amphetamines (amphetamine, methamphetamine), phencyclidine, adulterants, and alcohol (§ 26.31(d)(1)). This list of drugs for testing (excluding adulterants and alcohol) is referred to as a 5-panel test. Licensees can expand this list to include other controlled substances. However, while other drugs may be impairing, testing for them is forbidden under the FFD program (§ 26.31(d)(1)(i)). To identify scheduled drugs to be added to the drug panel, licensees may consult with local law enforcement authorities, hospitals, and drug counseling services to identify drugs with abuse potential that are being used in the geographical locale of the facility and by the local workforce that may not be detected in the minimum panel. When conducting post-event, follow-up, and for-cause testing, licensees may also test for any controlled substances an individual is suspected of abusing.[35] For testing of any additional drug or drug

[35] Note that the NRC's Drug Testing Program Frequently Asked Questions (https://www.nrc.gov/about-nrc/employment/drug-testing-faq.html) states, "The NRC random, applicant, follow-up, and voluntary programs test for the following five classes of drugs: marijuana, cocaine, opiates, phencyclidine (PCP), and amphetamines. When conducting injury/unsafe practices or reasonable suspicion testing, NRC may test for any drug(s) (including those mentioned above) identified in Schedule I or II of the Controlled Substances Act, as deemed necessary." The regulations at 10 CFR 26.31(d)(1)(i)(A) and 10 CFR 26.31(d)(1)(ii) state

metabolites, the licensee must establish testing procedures and cutoff levels that are certified in writing as being scientifically sound and legally defensible by an independent, qualified forensic toxicologist. The licensee's written policies and procedures must describe any additional drugs for testing (10 CFR 26.31(d)(i)(D)).

As the agency responsible for the Federal workplace drug-testing program, HHS periodically updates the federal drug-testing guidelines based on the most recent research and lessons learned from the Federal drug-testing program, as well as others who are regulated. The HHS Mandatory Guidelines (HHS Guidelines) have recently been expanded by SAMHSA to include 14 drugs in the 5-panel test, and U.S. Department of Transportation (DOT) has revised their requirements to be consistent with this revision (82 FR 52229). The expanded list includes two new amphetamines and four new semisynthetic opioids, and the cutoff levels for cocaine, amphetamine, and methamphetamine have also been lowered. The current NRC and revised DOT/HHS 5-panel drug test lists, along with their cutoff levels, are presented in Table 3-2. HHS-certified laboratories have the equipment and procedures in place for the expanded panel, and SAMHSA publishes the list of certified laboratories monthly (SAMHSA n.d.).

Table 3-2. Comparison of NRC and revised DOT/HHS 5-panel test cutoff levels.

5-Panel Drugs	Drugs on NRC's 5-Panel Test	NRC Confirmatory Cutoff Level (ng/mL) § 26.163(b)(1)	Drugs on HHS/DOT Expanded 5-Panel Test	HHS Confirmatory Cutoff Level (ng/mL) 82 FR 13
Marijuana (THC)	Marijuana metabolite (as delta-9-tetrahydro-cannabinol-9-carboxylic acid)	15	Marijuana metabolites (THCA)	15
Cocaine	Cocaine metabolite (as benzoylecgonine)	150	Cocaine metabolite (Benzoylecgonine)	100
Amphetamines	Amphetamine	500	Amphetamine	250
	Methamphetamine	500	Methamphetamine	250
			MDMA	250
			MDA	250
Opioids	Codeine	2000	Codeine	2000
	Morphine	2000	Morphine	2000
	6-acetylmorphine	10	6-AM (heroin)	10
			Hydrocodone	100
			Hydromorphone	100
			Oxycodone	100
			Oxymorphone	100
Phencyclidine (PCP)	Phencyclidine (PCP)	25	Phencyclidine	25

under certain conditions other drugs may be added to the panel of substances for testing if they are listed in Schedules I through V of Section 202 of the Controlled Substances Act (21 U.S.C. 812).

The FFD program has historically relied on HHS guidance to establish the technical requirements for urine specimen collection, testing, and evaluation, and has only deviated from the HHS guidelines for considerations that are specific to the nuclear industry. The FFD program requires use of HHS-certified laboratories, which are required by HHS to follow the HHS Guidelines in order to retain their certification. Prior to the added drugs and the cutoff levels that have been revised downward, the FFD program's drug testing was essentially consistent with the HHS Guidelines. Updating Part 26 to be consistent with the most recent HHS Guidelines would ensure that NRC regulations continue to be scientifically and technically sound, remain consistent with current HHS Guidelines, and avoid potential issues with certified laboratories that have to rely on older procedures or deviate from the current HHS Guidelines.

3.4.2 Drug-Testing Capabilities

Drug testing for legal prescription drug use is unlikely to be an effective means of discovering which drug, out of the many possible legal drugs, is causing an individual's impairment. Nevertheless, the FFD program has provisions for testing both the mandatory minimum substances and for expanding the list with additional drugs if certain conditions are met.

The FFD program requires that drug testing be done at laboratories certified by HHS under the requirements in the HHS Mandatory Guidelines for Federal Workplace Drug-Testing Programs (HHS Mandatory Guidelines) (§ 26.153(a)). HHS reports which laboratories are certified each month in a *Federal Register* notice (see Appendix F) (SAMHSA n.d.). These laboratories present a relatively stable resource capability that changes little month-to-month. The licensees must submit consolidated drug-testing performance data, including which HHS-certified laboratories they use, annually to NRC. Most licensees use NRC Form 891 for this reporting. Form 891 includes fields for reporting the licensees' primary and backup HHS-certified laboratories as well as space for the performance test sample supplier.[36]

The HHS-certified laboratories offer other medical testing services, including urine testing for additional drugs and drug metabolites. The available drug panels are limited and although the laboratories may have the knowledge and abilities to perform tests for many more drugs and drug metabolites, they may not have the HHS certification/approval required under § 26.153(a). Both the FFD program and the HHS Mandatory Guidelines require that for any drugs to be tested beyond the established 5-panel tests, the laboratory must develop, implement, and maintain detailed procedures for the drugs for which the laboratory is certified to test (§ 26.127(c), 82 FR 7920). Thus, to have one or more specimens tested for additional drugs in compliance with the FFD program, the licensee must do the following:

- Only test for drugs listed in Schedules I through V of CSA Section 202 (see Section 2.3.3 (§ 26.31(d)(i)(A))).
- Identify and use an HHS-certified laboratory for primary testing (which includes both initial and confirmatory tests) that is willing to or has already established the required standard operating procedures for that drug under the HHS Mandatory Guidelines (§ 26.153(b)).
- Identify another HHS-certified laboratory for backup testing (which includes both initial and confirmatory tests) that is willing to or has already established the required standard operating procedures for that drug under the HHS Mandatory Guidelines. If no backup testing laboratory

[36] Performance testing samples are program-generated samples used to evaluate laboratory performance. The HHS Mandatory Guidelines have detailed requirements for their composition and use.

is available for that drug and split specimen testing is needed, it would not be done at an independent laboratory as required (§§ 26.135(b), 26.165).

While many of the laboratories have instituted additional testing capabilities, it is difficult to determine which laboratories are certified to test for which additional drugs and, if one laboratory has been certified for a specific drug, it is not certain another laboratory is also certified for that drug. Because of these inherent challenges in expanding the list of drugs for testing, whenever the licensee has impairment concerns about an individual, it may be prudent to simply rely on a qualified medical professional's evaluation based on the individual's current ability with respect to his or her job duties.

3.4.3 Positive Drug Test

In the event a specimen has a confirmed positive test result, the MRO will collect additional information and evaluate whether the positive result could be from responsible use of legally prescribed medication (§ 26.183(c)). In this evaluation, the MRO can interview the donor and review relevant biomedical factors and medical records made available by the donor. Where a positive test result is found to be a policy violation, the licensee will determine what sanctions are applicable (see Section 3.3.4).

4.0 Safety-Sensitive Federal Agency Requirements for Prescription Drug Use in the Workplace

Federal agencies have established specific drug and alcohol testing requirements for industries that perform public safety and national security roles (SAMHSA 2019b). The Omnibus Transportation Employee Testing Act of 1991 requires drug and alcohol testing of all safety-sensitive transportation employees in aviation, trucking, railroads, mass transit, pipelines, and other transportation industries. Employers regulated by the following federal agencies are covered under the Omnibus Act:

- Federal Aviation Administration (FAA)
- Federal Motor Carrier Safety Administration (FMCSA)
- Federal Railroad Administration (FRA)
- Federal Transit Administration (FTA)
- National Highway Traffic Safety Administration (NHTSA)
- Pipeline and Hazardous Materials Safety Administration (PHMSA)
- U.S. Coast Guard (USCG).

The Administrator or Secretary of each of the above federal agencies defines which positions are identified as being safety-sensitive and has developed specific guidelines and procedures for complying with the Omnibus Act.

The U.S. Department of Defense (DoD) has developed its own set of regulations, Drug-Free Workplace (42 CFR 223.5), which requires that DoD contractors who have access to sensitive, classified information must maintain a drug-free workplace policy. DoD also has a drug-testing panel applicable to applicants for military service and for active military members.

Most Federal agencies, including those covered by the Omnibus Act, do not have formal federal requirements for reporting prescription drug and over-the-counter medication use, but they have issued various guidelines and policies. In addition, various employers receiving funding from the FTA have implemented specific prescription drug and over-the-counter use policies or employees are screened as part of their medical certification process. The FRA appears to be the only federal transportation agency that specifically requires medical evaluation of employees using prescription drugs. Two agencies (DOT and DoD) have expanded their drug-testing panel to include prescription drug opioids in accordance with the guidelines established by the HHS for Federal drug-testing programs for urine testing.

The following sections include information about regulations and procedures related to prescription drugs and over-the-counter medications specific to various federal agencies, including those within DOT and DoD covered under the Omnibus Act. Regulations for prescriptions and over-the-counter medications are more stringent in certain agencies, likely due to the risk, magnitude, and consequences of accidents that result in impacts on human health and safety associated with the type of employment and the nature of the job responsibilities.

4.1 U.S. Department of Transportation

DOT's regulations are codified at 49 CFR Part 40, which does not include specific language regarding reporting of prescription drugs or over-the-counter medications. Certain agencies within DOT employ workers performing safety-sensitive functions that are subject to DOT drug and alcohol testing, including the FAA, FMCSA, PHMSA, FRA, and FTA. Some of these agencies rely

on the general language of the DOT regulations, while other agencies have specific requirements described in more detail below.

The U.S. DOT Employer Handbook (DOE 2009) states that individuals performing safety-sensitive functions are allowed to use prescription medicine and over-the-counter drugs, but they must be prescribed for the individual by a licensed practitioner, and the prescribing/treating physician must make "a good faith judgment" that use of the substance "at the prescribed or authorized dosage level is consistent with the safe performance." The Handbook includes a best practice

> "…to assist your doctor in prescribing the best possible treatment, consider providing your physician with a detailed description of your job. A title alone may not be sufficient. Many employers give employees a written, detailed description of their job functions to provide their doctors at the time of the exam."

Furthermore, while taking prescription drugs and performing a safety-sensitive job is not prohibited, some "DOT agency regulations may have prohibitive provisions, such as medical certifications."

By statute, the DOT is required to follow the HHS Mandatory Guidelines for the drugs for which it tests in the transportation industry drug-testing program. DOT's final rule, which became effective on January 1, 2018, added four semisynthetic opioid substances (hydrocodone, hydromorphone, oxycodone, and oxymorphone) to its drug-testing program (82 FR 52229). These testing requirements are now codified at 49 CFR 40.85(d) and 40.87. Bills such as the *Fighting Opioid Abuse in Transportation Act*, S.2848, 115th Congress (2018) would require DOT to publish a final rule revising regulations for alcohol and controlled substances testing and would consider whether to add fentanyl in drug-testing policies, based on HHS review.

4.1.1 Federal Highway Administration

While the Federal Highway Administration (FHWA) regulations do not include specific information about prescription drug usage beyond those in the overarching DOT regulations, the Pilot Car Escort Training Manual (FHWA 2004), prepared by the Specialized Carriers and Rigging Association with FHWA funding, includes a statement that "pilot car escorts must not be under the influence of any medication, narcotic or alcohol that could potentially impair their ability to safely execute their responsibilities."

4.1.2 Federal Aviation Administration

Federal aviation regulations do not include any specific requirement for reporting of prescription drug or medication usage, but 14 CFR 61.53, 67.113, 67.213, 67.313, and 91.17 preclude flight crews from flying while having a condition or taking a medication that might affect flight safety. Under 14 CFR 61.53, Prohibition on Operations During Medical Deficiency, pilots are prohibited from being in command if they hold a medical certificate or are taking medication or receiving medical treatment for a medical condition such that the person is unable to meet the requirements for medical certification. Under 14 CFR 91.17, Alcohol or Drugs, the use of, "any drug that affects the persons faculties in any way contrary to safety" is prohibited. According to a 2014 U.S. Government Accountability Office (GAO) report, approximately 400,000 candidates apply each year for a pilot's medical certificate and complete a medical exam with an FAA-designated Aviation Medical Examiner to determine whether they meet FAA's medical standards (GAO 2014). From 2008 to 2012, about 10% of applicants were not certified by the Aviation Medical

Examiner, although about 8.5% of those applicants received a special issuance medical certificate after providing additional medical information to FAA (GAO 2014).

As a result of National Transportation and Safety Board (NTSB) recommendations issued to the FAA between 2000 and 2006, FAA developed a Guide for Aviation Medical Examiners and an informational brochure for pilots regarding the hazards of certain medications and flying (NTSB 2000), both of which are described in more detail below.[37]

FAA's Guide for Aviation Medical Examiners (FAA 2019) indicates that medical examiners should not issue medical certificates to applicants using certain types of medications and should advise applicants not to fly when using certain types of medications. The FAA's Do Not Issue category includes the following medication classes:

- angina medications
- anticholinergics (oral)
- cancer treatments, including chemotherapeutics, biologics, radiation therapy, etc., whether used for induction, "maintenance," or suppressive therapy
- controlled substances (Schedules I–V); an open prescription for chronic or intermittent use of any drug or substance
- diabetic medications not listed on the Acceptable Combinations of Diabetes Medications
- dopamine agonists used for Parkinson's disease or other medical conditions
- medications approved by the FDA less than 12 months ago
- hypertensive (centrally acting)
- malaria medication
- over-active bladder (OAB)/antimuscarinic medications
- psychiatric or psychotropic medications
- seizure medications
- smoking cessation aids
- steroids, high dose
- weight loss medications.

In addition to the medications on the Do Not Issue list, the Guide for Aviation Medical Examiners states that airmen should not fly while using any medication, prescription or over-the-counter, that carries a label precaution or warning that it may cause drowsiness or advises the user "be careful when driving a motor vehicle or operating machinery," noting that such medications "can cause impairment even when the airman feels alert and unimpaired" (FAA 2019).

[37] "The National Transportation Safety Board (NTSB) is an independent federal agency dedicated to promoting aviation, railroad, highway, marine, and pipeline safety. Established in 1967, the agency is mandated by Congress through the Independent Safety Board Act of 1974 to investigate transportation accidents, determine the probable causes of the accidents, issue safety recommendations, study transportation safety issues, and evaluate the safety effectiveness of government agencies involved in transportation" (NTSB 2014).

The FAA has also issued a safety brochure for pilots about use of medications when flying. The brochure indicates that pilots should ask their treating physician, pharmacist and Aviation Medical Examiner about side effects of medications and medical conditions while flying. The brochure also recommends "not to fly if you must depend upon the medication to keep the flight safe" (FAA n.d.). Similar precautions are identified regarding flying while taking over-the-counter medications and potential side effects of concern. The FAA suggests pilots do the following before flying:

- Consider the underlying condition that you are treating.
- Consider your reaction to the medication.
- Consider the potential for adverse reactions.

While the FAA does not publish a list of authorized medications,[38] the Aviation Medicine Advisory Service (AMAS) maintains a medication database of medications the FAA allows for use during flight, restrictions of medications, and those not usually allowed (AMAS n.d.). Pilot Medical Solutions also maintains a list of FAA-accepted medications (Pilot Medical Solutions 2019). FAR 61.53 prohibits acting as pilot-in-command or in any other capacity as a required pilot flight crewmember, while that person:

- knows or has reason to know of any medical condition that would make the person unable to meet the requirement for the medical certificate necessary for the pilot operation, or
- is taking medication or receiving other treatment for a medical condition that results in the person being unable to meet the requirements for the medical certificate necessary for the pilot operation.

The FAA's primary concern is whether the underlying medical condition being treated is compatible with safe flying (Yasuhara 2004). Medications typically used to treat such medical conditions are also commonly used continuously for effective treatment. These include, but are not limited to, anticoagulants, antiviral agents, anxiolytics (anti-anxiety), barbiturates, chemotherapeutic agents, experimental drugs, hypoglycemic medications, investigational drugs, mood-altering drugs, motion sickness medications, narcotics, sedating drugs, antihistamines, steroids, or tranquilizers.

In 2014, the NTSB published a report titled "Drug Use Trends in Aviation: Assessing the Risk of Pilot Impairment" (NTSM 2014). The report presented the results of the NTSB's analysis of the toxicology results of fatally injured pilots from 1990 and 2012 and identified the prevalence of illicit and prescription drugs and over-the-counter medications. The report makes it clear that NTSB is aware of the study's limitations because it only reveals recent drug use and not necessarily impairment at the time of the fatality due to the "complex relationships among positive toxicology findings, impairment, and accidents" and that NTSB recognizes the need for more research in this area (NTSB 2014:IX). Most of the pilots in the study were not involved with air carrier operations but were involved in general aviation operations. The most common potentially impairing drug used was the sedating antihistamine—diphenhydramine, which is an active ingredient in many over-the-counter cold medicines, sleep aids, and allergy formulations (NTSB 2014:IX). In addition, the study revealed that many of the pilots who had used potentially impairing drugs also did not have a current medical certificate, a concerning trend that has been increasing since 2005. The

[38] Experts commenting on the 2014 GAO study (mentioned in the introduction to this section), and NTSB have recommended that that the FAA create and make public lists of approved and unapproved drugs (GAO 2014 and NTSB 2014). FAA has historically resisted implementation of this recommendation because of concerns about the feasibility of keeping such a list current and comprehensive (NTSB 2014).

NTSB concludes the study with a variety of recommendations, two of which apply to FAA with regard to prescription drugs. One of them includes the recommendation that

> FAA develop, publicize, and periodically update information to educate pilots about the potentially impairing drugs identified in its toxicology test results of fatally injured pilots, and make pilots aware of less impairing alternative drugs if they are available" (NTSB 2014).[39]

The second recommendation relevant to FAA and prescription drug use includes the request for FAA to require pilots that are exempt from medical certifications to intermittently report to FAA about their flight hours and status as active pilots (NTSB 2014:5).

4.1.3 Federal Railway Administration

FRA regulations are codified at 49 CFR Part 219. The regulation states that "No employee who performs covered service may use a controlled substance at any time, whether on duty or off duty, except as permitted by § 219.103" (49 CFR § 219.102). Section 219.103 specifically requires the medical practitioner to evaluate a railway employee's prescription drugs and over-the-counter medication to ensure that they are consistent with the performance of safety-sensitive duties. The regulations do not prohibit the use of controlled substances prescribed or authorized by medical practitioners, under the following conditions:

- The treating medical practitioner or a physician designated by the railroad has made a good faith judgment, with notice of the employee's assigned duties and on the basis of the available medical history, that use of the substance by the employee at the prescribed or authorized dosage level is consistent with the safe performance of the employee's duties.
- The substance is used at the dosage prescribed or authorized.
- If the employee is being treated by more than one medical practitioner, at least one treating medical practitioner has been informed of all medications authorized or prescribed and has determined that use of the medications is consistent with the safe performance of the employee's duties (and the employee has observed any restrictions imposed with respect to use of the medications in combination).

In Skinner v. Railway Labor Executives' Association, 489 U.S. 602 (1989), the Supreme Court held that an alcohol or drug test conducted under FRA authority is a Fourth Amendment search, and in its determination of who should be subject to Part 219 testing, FRA must carefully balance public safety interests against individual privacy rights.

4.1.4 Federal Transit Administration

Relevant FTA regulations include 49 CFR Part 653, Prevention of Prohibited Drug Use in Transit Operations, and 49 CFR Part 655, Prevention of Alcohol Misuse and Prohibited Drug Use in Transit Operations. However, unlike the explicit references to prescription drug usage in the FRA regulations, neither of the FTA regulations includes specific information relevant to prescription drug usage.

In 2011, FTA issued a publication titled, "Prescription and Over-the-Counter Medications Tool Kit", (FTA 2011) a document that compiles best practices, procedures, policies, and training resources

[39] See also NIAAA (2014).

used by transit systems across the U.S. None of the policies discussed in the document are federally mandated. This document updates one completed by FTA in 2002, in part due to a NTSB directive issued in 2000 requiring all FTA grant recipients to investigate current policies regarding employee use of prescription drug and over-the-counter medications that could jeopardize public safety. The directive also directed the FTA to educate operators about risks associated with prescription drugs and over-the-counter medications. Between 2002 and 2011, NSTB issued additional requirements "to develop a standardized methodology to collect the information on the role Rx [prescription drug]/over-the-counter medications play in transit industry fatal accidents…" (FTA 2011:2). FTA made a concerted effort to collect data from various transit systems and transit databases, resulting in the finding that as of 2011 almost two-thirds of the participating transit systems have updated their Substance Abuse Policies to address prescription drugs and over-the-counter medications. FTA recommends that a prescription drug/over-the-counter medication program should also consider and address medical conditions that can also result in adverse impacts on transit safety. At a minimum, transit systems should ensure that the prescription drug and over-the-counter medication procedure includes a requirement for employees to report, authorize, and monitor drug use, and obtain input from a physician about their use of prescription drugs and over-the-counter medications and the potential for such use to conflict with safety-sensitive duties.

The 2011 report includes a list of medical conditions that may impair driving, a list of medications and associated side effects that can impair driving, examples of best practices and FFD policies from nine transit systems (e.g., Indiana DOT, Maryland Transit Administration), a list of recommended components of an ideal policy, and an overview of different methods used for implementing prescription drug and over-the-counter medication policies. Concerns regarding the implementation of such policies focused on the cost of extra paperwork in the absence of a federal mandate, concerns about employee privacy, and concerns about employee abuse of policy.

Of the examples of best practices provided, they can be summarized into three different "policy approaches" (FTA 2011:II-4):

- Employee self-determines ability to safely perform duties.
- Employer requires authorization by physician/MRO.
- Issue a list of medications as a guide for those that must be avoided or that may require evaluation.

A 2012 FTA newsletter includes a list of the "Ten Most Common Prescription Medications Used by Transit Employees" (FTA 2012). The article cautions transit employees to work with their physicians to disclose all medications, including drug combinations, to ensure their use does not interfere with the employee's ability to perform safety-sensitive duties. The top 10 are

- antihypertensives
- antihyperlipidemics
- ASA-cardiac
- antidiabetic oral
- NSAIDS
- GERD/H2 blockers
- antihistamines
- antidepressants
- analgesics (non-narcotic)
- asthma/bronchodilators.

In 2013, The Transit Rail Advisory Committee for Safety (TRACS) Working Group issued a document titled, "Defining Standards and Guidance for Establishing Policies to Govern the Use of Prescription and Over-the-Counter Medications by Safety-Sensitive Transit Personnel" (TRACS 2013), which provides a list of recommendations for the FTA Drug and Alcohol Program Manager

regarding prescription drug/over-the-counter medication policies, training and accident/incident investigations.

4.1.5 Pipeline and Hazardous Materials Safety Administration

PHMSA's drug and alcohol testing regulations are at 49 CFR 199. These regulations require operators of pipeline facilities to test covered employees for the presence of prohibited drugs and alcohol. However, the regulations do not address testing associated with prescription drugs prescribed by a doctor.

4.1.6 Federal Motor Carrier Safety Administration

FMCSA's regulations are at 49 CFR 382. "Controlled substance use" (49 CFR 382.213) states that, "Although the driver has a legal prescription, he/she may be disqualified if the medication could adversely affect the driver's ability to drive a CMV [commercial motor vehicle] safely" (FMCSA 2017). According to an FCMSA Frequently Asked Question (FAQ) document, "[a] driver cannot take a controlled substance or prescription medication without a prescription from a licensed practitioner." If a driver uses a drug identified in 21 CFR 1308.11 or any other substance such as amphetamine, a narcotic, or any other habit-forming drug, the driver is medically unqualified. An exception is that "the prescribing doctor can write that the driver is safe to be a commercial driver while taking the medication (49 CFR § 391.41). In this case, the Medical Examiner may, but does not have to certify the driver." Anti-seizure and methadone usage are specifically called out as medically disqualifying.

4.1.7 National Highway Traffic Safety Administration

While it is also a DOT agency, the NHTSA differs from the above agencies because it does not regulate or employ workers to perform safety-sensitive functions. NHTSA's mission to is to save lives, prevent injuries, and reduce economic costs due to road traffic crashes through education, research, safety standards, and enforcement.[40] In 2019, NHTSA started the "There's More Than One Way to Be Under the Influence" to show how legally obtained and commonly used drugs and medications can affect a user's ability to drive safely (NHTSA n.d.-b). The campaign included the following statements relevant to prescription drugs and over-the-counter medications:

- Some prescription drugs can induce drowsiness, cause nausea, affect judgment, and lessen coordination, all of which can prove fatal when driving.
- Over-the-counter drugs may cause drowsiness, dizziness, nausea, irregular heartbeat, or shakiness. Users should avoid operating motor vehicles if they are experiencing any side effects from the medication.
- Prescription drugs such as opioids, sedatives, muscle relaxants, and some antidepressants have been associated with increased crash risk.
- Some medications may not impair you on their own, but if taken with a second medication or with alcohol, may cause impairment.
- Violating state DUI [driving under the influence] laws that make it illegal to drive impaired by any substance can result in arrest. This includes prescription drugs and over-the-counter medications.

[40] For more information see the NHTSA website at https://www.nhtsa.gov/.

4.2 United States Department of Defense

DoD has a robust drug detection and deterrence policy as described in DoD policies and programs: DoD Instruction 1010.04 "Problematic Substance Use by DoD Personnel", DoD Instruction 1010.01 "Military Personnel Drug Abuse Testing Program", and DoD Instruction 1010.09 "DoD Civilian Employee Drug-free Workplace Program." DoD's drug-testing panel is applicable to applicants for military service and active military members.

DoD's drug detection program includes prevalence testing to monitor the use of illicit drugs that are not on the current testing panels so that DoD can identify trends of drug abuse among military personnel (DoD 2018). DoD modifies the prevalence drug-testing menu in response to low positive rates, emerging drugs, and societal drug-use patterns (such as the recent rise in opioid use and availability of synthetic cannabinoids) (Platteborze and Martin 2017).[41] In response to the prevalence testing program, in March 2017, DoD expanded their drug-testing panel to include heroin, codeine, morphine, hydrocodone, oxycodone, hydromorphone, oxymorphone, and synthetic cannabinoids and benzodiazepine (Ferdinando 2017). In March 2019, DoD directed service-related labs to test for fentanyl and its metabolite norfentanyl and, in the case of positive tests, to direct MROs to determine when the use is associated with a legitimate prescription (Leldhom 2019).

A review of the DoD drug detection and deterrence policies and programs identified above reveals that there are no requirements for reporting prescription drugs other than needing to self-report if the drug use is associated with a disqualifying medical condition. Disqualifying medical conditions for appointment into the Military Services include use of certain prescription drugs associated with underlying conditions, including headaches and migraines, restless leg syndrome, airway hyperresponsiveness, dyspepsia, gastritis, duodenitis, constipation, or irritable bowel syndrome "that may reasonably be expected to interfere with military duty."[42]

4.3 United States Coast Guard

Specific medical and physical requirements for the USCG are codified in 46 CFR 10.302 (USCG 2005, 2016). The USCG, which operates under the U.S. Department of Homeland Security (DHS) during peacetime, issues medical waivers if the medication poses "no significant risk"). As part of the medical exam, medication that may "impair cognitive ability, judgment or reaction time" must be documented.

On April 25, 2016, the USCG issued a change notice to their Medical and Physical Evaluation Guidelines for Merchant Mariner Credentials, Navigation and Inspection Circular (NVIC) 04-08, COMDTPUB 16700.4. A few sections contained in these guidelines pertain to prescription drug and over-the-counter medication use, including the recommendation that medical practitioners ask applicants about use of prescription drugs and over-the-counter medications. Additional guidance includes the recommendation that mariners seek medical advice before taking medications and read manufacturer warnings and labels prior to working while taking medications. Mariners are required to disclose all prescription and over-the-counter medication as part of the

[41] In 2006, oxycodone and oxymorphone were added and were followed by hydrocodone and hydromorphone in 2012. In 2013, benzodiazepines were added and were followed by synthetic cannabinoids in 2014. As of 2017, five different benzodiazepines and eight synthetic cannabinoids are tested (Platteborze and Martin 2017).

[42] See https://www.esd.whs.mil/Portals/54/Documents/DD/issuances/dodi/613003p.pdf?ver=2018-05-04-113917-883\.

application and medical certification process if their job duty requires a medical exam. Several medications are considered to be disqualifying for issuance of a medical certificate, but mariners may seek consideration for a waiver. Medications that may be considered to be disqualifying are listed below. If medications are being used, mariners will require additional medical review to determine if use is considered to be disqualifying. Potentially disqualifying medications include the following:

- antidepressants
- anti-motion sickness agents
- antipsychotics
- anticonvulsives
- antihistamines, allergy medications
- barbituate medications
- benzodiazepine medications
- cough and cold medicines
- stimulant medications
- sleep aids
- legally prescribed controlled substances
- medical use of hallucinogens
- muscle relaxants.

The document identifies additional medications that may have associated side effects that affect a mariner's ability to safely and effectively perform duties or that may increase the possibility of the user being sick while at sea. These medications include the following:

- CNS depressants/stimulants
- agents that increase the likelihood of sudden incapacitation
- medications that impair vision.

Causes of potential adverse effect while "under way" include the following:

- medications that can cause prolonged bleeding
- cessation of medication use
- long-term antibiotic use
- cancer treatments
- medications used at individual discretion.

Opioids, benzodiazepine medications, non-benzodiazepine sedative hypnotic medications, and barbiturate medications will not be waived except under exceptional circumstances. The waiver process in these circumstances is outlined in detail in the document and includes neuropsychological/neurocognitive testing.

5.0 Employee Protection and Legal Considerations

The implementation of NRC FFD program and prescription drug-use policy by licensees and entities is intended to ensure that individuals employed in safety- and security-sensitive positions are fit for duty without conflicting with the legal protection and employment provisions of prevailing laws that afford individuals with protection against discrimination and/or unauthorized disclosure of private medical information. In this section, we provide a discussion of the provisions of laws such as the ADA and the HIPAA, their interface with NRC FFD policy provisions, and the outcomes of recent litigation involving prescription drug use and prescription drug-related impairment in the workplace to further clarify the reach of workplace prescription drug policy and the rights and limitations of employers and covered individuals employed by licensees and entities.

5.1 The Americans with Disabilities Act

Title I of the Americans with Disabilities Act of 1990 (ADA) (Pub. L. 101-336, July 26, 1990) and the ADA Amendment Act of 2008 (ADAAA) (Pub. L. 110-325, Sept 25, 2008) provide protections for individuals with disabilities from employment discrimination on the basis of their disabilities in all employment practices. The U.S. Equal Employment Opportunity Commission (EEOC) is the Federal agency that administers the ADA[43] and provides regulation and guidance regarding ADA implementation and enforcement.

5.1.1 ADA Definitions: Disability, Impairment, and Qualified Individuals

An individual taking prescription drugs to treat medical conditions might be considered a qualified individual with a disability if certain conditions are met in accordance with the provisions of the ADA. The ADA provides a three-pronged definition for disability in 29 CFR Part 1630.2(g)(1) where a disability refers to:

> (A) a physical or mental impairment that substantially limits one or more major life activities of such individual;
>
> (B) a record of such an impairment; or
>
> (C) being regarded as having such an impairment.

According to ADAAA, major life activities “include but are not limited to caring for oneself, performing manual tasks, seeing, hearing, eating, sleeping, walking, standing, lifting, bending, speaking, breathing, learning, reading, concentrating, thinking, communicating, and working” (§1630.2(i)(1)(i)). Major life activities also include “the operation of a major bodily function, including but not limited to, functions of the immune system, normal cell growth, digestive, bowel, bladder, neurological, brain, respiratory, circulatory, endocrine, and reproductive functions. The operation of a major bodily function includes the operation of an individual organ within a body system” (§1630.2(i)(1)(ii)).

Although the ADA does not list all the covered impairments, the EEOC defines a physical or mental impairment as “any physiological disorder or condition, cosmetic disfigurement, or anatomical loss affecting one or more body systems, such as neurological, musculoskeletal,

[43] Unless explicitly stated, hereafter, the term ADA refers to the ADA of 1990, as amended by the ADAAA of 2008.

special sense organs, respiratory (including speech organs), cardiovascular, reproductive, digestive, genitourinary, immune, circulatory, hemic, lymphatic, skin and endocrine…or any mental or psychological disorder, such as intellectual disability (formerly termed mental retardation), organic brain syndrome, emotional or mental illness, and specific learning disabilities" (§ 1630.2(h)).

Further, the duration of an impairment is not a determinant of whether the impairment is considered a disability, as § 1630.2(j)(1)(vii) states, "An impairment that is episodic or in remission is a disability if it would substantially limit a major life activity when active." In addition, a disability must be determined "without regard to the ameliorative effects of mitigating measures" (e.g., medication, medical equipment, devices, prosthetics, assistive technology) (§1630.2(j)(1)(vi)). Moreover, the determination of whether an impairment substantially limits a major life activity requires an individualized assessment (§ 1630.2(j)(1)(iv)), and the effects of an impairment lasting or expected to last less than six months can be substantially limiting, and thus could be a disability (§ 1630.2(j)(1)(ix)).

Overall, the intent of the ADAAA was to better enable people with disabilities to obtain protection than previously under the ADA. The amendment shifted the focus from individuals bearing the burden of proof for having a disability to covered entities demonstrating ADA compliance and the investigation regarding whether disability-based employment discrimination occurred (§1630.1(4)).

5.1.2 Qualified Individuals with a Disability under the ADA

A qualified individual with a disability, under Title I of the ADA employment protection provisions, must meet the definition of disability as discussed in Section 5.1.1 and have the "legitimate skill, experience, education, or other requirements of an employment position that he or she holds or seeks," or satisfy "job requirements for educational background, employment experience, skills, licenses, and any other qualification standards that are job-related" (EEOC 2019a) and can perform the essential function of the position with or without reasonable accommodation (EEOC n.d.). Thus, an important qualification criterion is that the ability of an individual with a disability to perform the essential function of a job and satisfy the requirements of the position does not depend on having reasonable accommodation.

In the pre-employment stage, employers typically publish job postings with descriptions of job duties, and requirements for education, skill, and work experience, etc. Employers might also require certain tests and selection procedures to evaluate job applicants and/or incumbent employees to assess whether they can perform the essential function of the job. These job descriptions, tests, and selection procedures are example sources of information that can be used to characterize the essential job function of a position. The ADA does not prohibit an employer from requiring these tests and selection procedures as long as they are not used to screen out job applicants and employees on the basis of their disabilities or other attributes, such as gender, race, and age, thereby violating Federal anti-discrimination laws, such as the ADA (disability-based discrimination), Title VII of the Civil Rights Act of 1964 (discrimination on the basis of race, color, religion, sex, or national origin) and the Age Discrimination in Employment Act (age discrimination) (EEOC 2010).

5.1.3 ADA Protection Involving Drug Use

Whether an individual is considered an individual with a disability also depends on the nature of his/her drug use. Under the ADA, individuals currently engaging in illegal use of drugs do not meet the definition of an individual with a disability (28 CFR 36.104). The ADA states,

> Illegal use of drugs means the use of drugs the possession or distribution of which is unlawful under the Controlled Substances Act, as periodically updated by the Food and Drug Administration. This term does not include the use of a drug taken under the supervision of a licensed health care professional, or other uses authorized by the Controlled Substances Act or other provisions of Federal law (29 CFR 1630.3 (a)(2)).

This indicates that individuals with disabilities who are taking legally prescribed medications under the supervision of a treating physician or licensed healthcare provider are considered qualified individuals.

The term—illegal use of drugs—captures both the use of illegal drugs that are controlled substances (e.g., heroin, phencyclidine, lysergic acid diethylamide [LSD]) and the illegal use or misuse of prescription drugs that are controlled substances (e.g., morphine, oxycodone, methadone) (USCCR 2010). Judicial interpretation of illegal use of drugs in disability discrimination cases seems to be consistent with this broad reach of the term. For example, the court in Nielsen v. Moroni Feed Co. stated, “There is no doubt that, under the ADA, illegal drug use includes the illegal misuse of pain-killing drugs which are controlled by prescription as well as illegal street drugs like cocaine” (Nielsen v. Moroni Feed Co., 162 F.3d 604, 611, fn. 12 (10th Cir. 1998)). Possible examples of illegal use of prescription drugs could include use without a legitimate prescription (taking someone else’s prescription or using a fraudulent prescription) or use in excess of the prescribed dosage.

In addition, the ADA defines the meaning of “current illegal use” by stating, “Current illegal use of drugs means illegal use of drugs that occurred recently enough to justify a reasonable belief that a person's drug use is current or that continuing use is a real and ongoing problem” (28 CFR 36.104). This suggests that the interpretation of what constitutes current use will need to be made in view the specific context and evidence presented in each case. This also indicates that ADA provisions do not exclude individuals who are recovering from such use (e.g., having completed or participating in supervised drug rehabilitation programs) and no longer engaging in illegal use (29 CFR 1630.3(b)(1)(2)).

5.1.4 Disability-Related Inquiries and Medical Examinations under the ADA

Under the ADA, employers have obligations to comply with disability-related provisions and need to identify what information can and cannot be obtained from individuals with regard to their disabilities at different stages of the employment process.

The ADA prohibits an employer from making disability-related inquiries of job applicants during the pre-offer stage. During the post-offer stage, an employer is not prohibited from making disability-related inquires or requiring medical examinations if such inquiries and examinations are required for all new employees in the same job category. In this scenario, the inquiries and examinations need not be job-related (EECO 2019b). However, after an individual becomes an employee, employers may make disability-related inquiries only if they are job-related and consistent with the business necessity of the employer.

An employer may request medical information from an employee if an employer has objective evidence to reasonably believe that an employee cannot perform the essential functions of his/her job and/or will pose a direct rather than a perceived threat because of a medical condition (i.e., consistent with business necessity); or if an employee requests reasonable accommodation but the disability or the basis for such a request is not obvious to the employer. In the latter case, the employer can request the employee to provide sufficient medical documentation to substantiate the condition that gives rise to the reasonable accommodation request. Thus, an employer may not ask any employee about his/her current prescription drug use unless the employer reasonably believes an employee is impaired, which poses a real and direct threat to the employer's business, and/or the employee's impairment compromises his/her ability to perform the essential job function. For example, airlines could require pilots to report medication use that impairs their ability to fly; NRC-licensed operators and senior operators are required to undergo biennial medical examination to ensure appropriate work restrictions are in place for potentially impairing health conditions and to ensure the health conditions will not pose a direct threat with grave consequences for national security and public health and safety. Employers must keep such medical information confidential and keep it separate from employees' employment records.

5.1.5 Litigation Involving ADA Violations and Prescription Drug Use in the Workplace

As discussed in Section 5.1.3, the ADA employment provisions do not extend to individuals currently engaging in illegal use of drugs. Qualified individuals with disabilities taking legally prescribed medication in a legally prescribed manner—under the supervision of licensed healthcare professional—are eligible for ADA anti-discrimination protection. ADA also protects qualified individuals who have histories of past drug addiction or are recovering from drug addiction against discriminatory treatment and practices due to their disabilities.

For individuals working in safety- and security-sensitive industries, the employers typically need to strike a balance between ensuring the workplace is free from the influence of drugs and the workforce is not impaired and the legal obligation to comply with applicable laws such as the ADA. A host of recent litigations involving prescription drug use in the workplace and disability-based discrimination continues to clarify the legal boundaries and constraints for employers and employees.

In EEOC v. Foothills Child Development Center, Inc., Civil Action No. 6:18-cv-01255-AMQ-KFM), Foothills Child Development Center terminated an employee after the employee disclosed his participation in a medication-assisted treatment program and that he was using a legally prescribed medication as part of the treatment. The center terminated the employee without conducting any individualized assessment to determine if the prescription medication impaired the employee's ability to perform the essential job function. The EEOC found the center in violation of the ADA and that it had discriminated the individual on the basis of his disability. The center agreed to compensate the individual and amend its drug policy to incorporate provisions for individuals taking legal prescription medication in a lawfully prescribed manner (EEOC 2018b).

In a similar case, EEOC v. M.G. Oil Company d/b/a Happy Jack's, 4:16-cv-04131-KES (D. S.D.), M.G. Oil Company rescinded a job offer upon discovering a job applicant's drug test that showed "lawful presence" of a legally prescribed medication. Further, the company policy required all employees to report all medication use (over-the-counter and prescription medication) regardless of their actual effects on employees' job performance. The EEOC found M.G. Oil in violation of the ADA and reached a settlement with the company. M.G. Oil was required to compensate the wrongfully dismissed job applicant and to amend its drug policy to require employees to report

prescription medication only if the company has a reasonable suspicion that the medication would impair employees' job performance (EEOC 2018c).

EEOC v. Bell Leasing, Inc. (Civil Action No. 2:16-cv-02848-DKD) also resulted in similar sanctions for an employer for wrongfully denying a qualified job applicant of employment due to legal prescription medication use and refusing to make reasonable accommodation where no undue hardship was found. EEOC commented,

> Blanket exclusion policies based on drug test results harm job applicants and employers. The ADA requires a case-by-case evaluation of applicants with disabilities to make sure employers assess these applicants on their merits (EEOC 2017).

In a 2012 lawsuit, (Civil Action No. 1:09-cv-00059), EEOC alleged Dura Automotive Systems Inc. violated the ADA provisions by penalizing employees who tested positive for legal prescription medications that were taken in a legally prescribed manner, requiring these employees to disclose their medical conditions associated with the drug use, and requiring them to discontinue medication use if they were to keep their employment with the company. The EEOC found Dura in violation of multiple ADA provisions, including conducting drug testing that was unrelated to the job and not consistent with business necessity, making medical inquiries and conducting medical examinations impermissible under the ADA, and failing to keep employee's medical information confidential. As a result of the consent decree, Dura was required to produce a written ADA compliant drug-testing policy, provide ADA training to Human Resources management, and the CEO of Dura was required issue a no-retaliation statement for individuals who complained about the company's drug-testing practices.

EEOC brought a lawsuit against Loflin Fabrication LLC (EEOC v. Loflin Fabrication LLC, Civil Action No. 1:18-cv-00813) for violating the ADA by requiring all employees provide a copy of all medication prescriptions and firing an employee who disclosed legal medication use without providing a copy of the prescription to the company despite the lack of evidence of impairment associated with drug use and negative drug test results. The EEOC reiterated that the employers are prohibited from making such inquiries that could

> reveal disability-related information unless employers can establish that there is a business necessity for such inquiries based on each employee's particular job duties… Hard-working employees should not lose their jobs simply because they are unwilling to disclose private health information that has nothing to do with their ability to do their jobs (EEOC 2018a).

ADA employment provisions do not apply to individuals with disabilities who are unable to perform the essential job functions with or without reasonable accommodation because they are not considered qualified individuals. In the workplace, qualified individuals with disabilities are held to the same performance standards as other individuals without such disabilities in the same job category. The ADA does not reduce the standard of professional conduct or performance for people with disabilities. Employers can impose disciplinary action on employees with disabilities for poor performance, which could include termination of employment. A 2019 case, Connelly vs. WellStar Health System Inc. (No. 18-11217 (11th Cir. 2019)), provides added confirmation that being unable to perform the essential function of a position desired or held disqualifies an individual from ADA protection and results in failure to establish a claim of discriminatory termination on the basis of disability as a matter of law.

5.1.6 Implication for Fitness for Duty

Whereas the ADA protects qualified individuals from disability-based discrimination in employment and prohibits employers from making disability-related inquiries and conducting medical examinations unless they are job-related and are consistent with business necessity, there are circumstances under which the ADA provisions might interface with legally mandated requirements by other Federal laws such as the NRC FFD regulations and those of the DOT, which might require clarification regarding the limits of the ADA vis-à-vis those other Federal laws.

In Silver v. Entergy Nuclear Operations, Inc. (Kapusta n.d.), the court's summary judgment ruled in favor of a NPP operator regarding disability-based discrimination charges brought forth by an individual previously employed as an armed security guard who alleged his former employer wrongfully regarded him as having a disability, failed to make reasonable accommodation, and illegally terminated his employment. While employed at the plant, the individual had been taking prescription anti-anxiety medication. After experiencing an episode of hallucination while on the medication, the security guard underwent a psychological evaluation and fitness determination at work per FFD and access authorization requirements. The psychologist determined the individual to be not fit for duty and recommended that his unescorted access authorization be revoked. The security guard's employment was subsequently terminated. The court states that armed security guards at NPPs are legally required to be fit for duty and being fit for duty is the prerequisite for unescorted access authorization, which is an essential job function. Thus, being unfit for duty renders the individual unqualified for the job and ineligible for the protective provisions of the ADA.

A recent appellate court opinion reflects the interplay between the provisions of ADA and the NRC's FFD regulations. In McNelis v. Pennsylvania Power & Light Company (2017), the court affirmed the summary judgment in favor of an NPP against the claims of ADA violation made by a former employee who worked as a security officer at the plant. The former employee had drug and alcohol issues, the severity of which prompted a coworker to report his behavior to plant management. The former employee underwent a fitness determination conducted by a licensed, third-party psychologist contracted by the plant and was determined to be not fit for duty. Based on the results, he was stripped of his access authorization and later his employment was terminated after his internal appeal was denied.

The appellate court's opinion highlighted several important legal considerations regarding the ADA-FFD interplay:

- The ability to obtain and maintain access authorization and being fit for duty is essential to the job as a plant operator in a NPP; thus losing one's access authorization or being determined to be unfit for duty would make an individual an unqualified person under the ADA, even if the individual has the appropriate education, training, skills, and experience or is "otherwise qualified to perform the essential function of the job" (see also, Wetherbee vs. S. Nuclear Operating Co., 2010 WL 11428172).
- Case law has established that "a legally-defined job qualification is by its very nature an essential function of the ADA" (Brickers v. Cleveland Bd. Of Educ., 145 F.3d 846, 850 (6th Cir. 1998)). The court's decision in McCoy v. Pa. Power and Light Co., 933 F. Supp. 438, 444 (M.D. Pa. 1996) affirms that the ability to meet the NRC's "legally dictated fitness-for-duty program" is "by its very nature an essential function." Thus, not meeting the FFD program's legally mandated requirements renders an individual unable to perform the essential function of a position, and thus ineligible for ADA protections.

- The Supreme Court's decision in Albertson's Inc. v. Kirkingburg, 527 U.S. 555 (1999) states, "when Congress enacted the ADA, it recognizes the federal safety rules would limit application of the ADA as a matter of law." Licensees and other entities subject to NRC regulations and employers subject to DOT regulations have "an unconditional obligation" to comply with these regulations and the actions taken by these employers in meeting the legal requirements were not "insisting up a job qualification of its own devising."
- The court recognized the security- and safety-sensitive nature of NPPs and the merit in NRC's policy judgment to conduct medical examinations that might be prohibited under the ADA in other contexts. The appellate court opinion asserts, "the premise that the ADA applies differently to professions that implicate the public welfare is as essential as it is unremarkable."
- The review procedures inherent in the NRC regulations (e.g., 10 CFR 73.56(1); 10 CFR 26.39) provide individuals with opportunities to provide additional relevant information regarding a decision that was based on an impartial and independent review by internal management. The review procedures are an important measure to ensure that due process is in place for individuals facing a potential policy violation.

5.2 Health Insurance Portability and Accountability Act

Enacted in 1996, the HIPAA (Pub. L. 104–191) was promulgated to enhance healthcare industry efficiency, improve healthcare insurance coverage continuity and portability, and protect and secure individuals' health information (Alder 2017). Title II of HIPAA requires the HHS to establish national standards for implementing the Administrative Simplification provisions of HIPAA. To that end, the HHS has issued the Privacy Rule, Security Rule, Transactions and Code Set Rule, Unique Identifiers Rule, and Enforcement Rule. In particular, the HIPAA Privacy Rule, also known as the *Standards for Privacy of Individually Identifiable Health Information*, regulates the use and disclosure of protected health information by covered entities and business associates; the Security Rule, also known as the *Security Standards for the Protection of Electronic Protected Health Information,* regulates the security of electronic health information. The HHS Office for Civil Rights is responsible for enforcing the Privacy and Security Rules.

5.2.1 Applicability of HIPAA

HIPAA privacy rules apply to covered entities and business associates (HHS 2017a). Under the HIPAA, three types of entities are covered:

- Health plans, such as insurance companies, health maintenance organizations, employer-sponsored health plans, Government-paid healthcare programs such as Medicare, Medicaid, and veteran's health programs; a group health plan sponsored by an employer is also considered a covered entity although the employer itself might not be. [44]

[44] HHS states, "A "group health plan" is one type of health plan and is a covered entity (except for self-administered plans with fewer than 50 participants). The group health plan is considered to be a separate legal entity from the employer or other parties that sponsor the group health plan. Neither employers nor other group health plan sponsors are defined as covered entities under HIPAA. However, the Privacy Rule does control the conditions under which the group health plan can share protected health information with the employer or plan sponsor when the information is necessary for the plan sponsor to perform certain administrative functions on behalf of the group health plan. See 45 CFR 164.504(f). Among these conditions is receipt of a certification from the employer or plan sponsor that the health information will be protected as prescribed by the rule and will not be used for employment-related actions." See https://www.hhs.gov/hipaa/for-professionals/faq/499/am-i-a-covered-entity-under-hipaa/index.html.

- Healthcare clearinghouses, which are "organizations that process nonstandard health information to conform to standards for data content or format, or vice versa, on behalf of other organizations" (HHS 2017a). Examples of healthcare clearinghouses can include "a public or private entity, including a billing service, repricing company, community health management information system or community health information system, and 'value added' networks" (NIH 2007).
- Healthcare providers, such as doctors, clinics, dentists, chiropractors, pharmacies, nursing homes, and psychologists.

Under HIPAA, a business associate refers to "a person or entity that performs certain functions or activities that involve the use or disclosure of protected health information on behalf of, or provides services to, a covered entity" (HHS 2019). The functions and activities performed by a business associate could include processing claims, data analysis, billing, and repricing. A detailed definition for "covered entity" and "business associate" is provided in 45 CFR 60.103. The HIPAA Privacy Rule does not apply to organizations and/or individuals that do not meet the definition of a covered entity or a business associate.

The HIPAA Privacy Rule mandates the protection of individually identifiable health information "held or transmitted by a covered entity or its business associate, in any form or media, whether electronic, paper, or oral" (45 CFR 160.103). Individually identifiable health information (also known as protected health information) refers to the "information, including demographic data, that relates to:

1. the individual's past, present or future physical or mental health or condition,
2. the provision of health care[45] to the individual, or
3. the past, present, or future payment for the provision of health care to the individual and that identifies the individual or for which there is a reasonable basis to believe it can be used to identify the individual" (45 CFR 160.103). Examples may include names, addresses, social security numbers, and dates of birth.

The Security Rule established the national standards for protecting an individual's personal health information that covered entities produce, receive, use, and maintain in the *electronic* form, and mandates that these covered entities have appropriate safeguards in place to ensure "information confidentiality, integrity and security" (HHS 2017c).

5.2.2 HIPAA Provisions and the Workplace

As mentioned in the previous section, organizations that do not meet the definition of a covered entity or business associate are not required to comply with the HIPAA Privacy Rule. Further, according to the HHS, the Privacy Rule does not apply to medical records associated with employment even if such records contain health-related information. The HHS states, "In most cases, the Privacy Rule does not apply to the action of an employer" and "Generally, the Privacy Rule applies to the disclosures made by your healthcare provider, not the questions your employer may ask" (HHS 2017b). The Privacy Rule does not prohibit an employer from asking an

[45] Healthcare means "care, services, or supplies related to the health of an individual. Health care includes, but is not limited to, the following: Preventive, diagnostic, rehabilitative, maintenance, or palliative care, and counseling, service, assessment, or procedure with respect to the physical or mental condition or functional status, of an individual or that affects the structure or function of the body; Sale or dispensing of a drug, device, equipment, or other item in accordance with a prescription" (45 CFR 160.103).

employee to provide health information regarding work-related requests such as sick leave, worker's compensation, health insurance, and reasonable accommodation. Further, an employer is not prohibited by HIPAA from directly contacting an employee's physician to obtain such information. However, the healthcare provider is prohibited by HIPAA Privacy Rule from disclosing such information to the employer without the employee's authorization, which is a detailed document that gives covered entities (e.g., healthcare providers in this case) the permission to use or disclose protected health information to a third party (e.g., an employer) for purposes other than treatment, payment, or healthcare operations (HHS 2013).

For workplace drug testing, if the entities and individuals involved in the drug testing, such as drug-testing collection facilities, laboratories, MROs, substance abuse professionals/experts, are covered entities or business associates under HIPAA, they must obtain HIPAA-compliant authorization from the employees subject to drug testing before executing the tests and releasing test results to the employers, unless Federal laws require no written authorization from the donor to use or disclose otherwise protected health information (45 CFR 164.512(a)). It is worth noting that the DOT has issued clarification to explicitly state that HIPAA compliance does not apply to employers and their service agents subject to the DOT drug and alcohol testing requirements (DOT 2016). If an employer requires medical information regarding an employee's substance abuse rehabilitation program as part of an employment continuation agreement and if the program provider is a covered entity under HIPAA, the employer will need to obtain the employee's HIPAA-compliant authorization to allow the release of protected health information from the program provider to the employer. Thus, unless an employer is a covered entity or business associate, the employer has no HIPAA compliance obligation for obtaining employees' HIPAA-compliant authorization for releasing workplace drug test information. However, other laws (e.g., state drug-testing laws) might nonetheless require employees' consent for conducting workplace drug testing and releasing test results to employers (Alere Toxicology 2016; Origin Diagnostics 2012).

The HIPAA Privacy Rule also stipulates that disclosure of protected health information without authorization is permitted for certain public health activities to ensure public health and safety. General public health activities include disease prevention and control and injury and disability reporting by public health authorities (e.g., FDA, CDC, OSHA). Additional types of public health activities include reporting of child abuse or neglect; quality, safety, or effectiveness of FDA-regulated products; persons at risk for contracting or spreading communicable diseases; and workplace medical surveillance (HHS 2003).[46] Therefore, an employer can legally require the release of protected health information about employees (e.g., work-related injury or illnesses or workplace medical surveillance) without authorization to comply with OSHA requirements (45 CFR 164.512(a) and (b)) and those of the Mine Safety and Health Administration (MHSA) (30 CFR Part 50). In addition, it is important to note that the HIPAA Privacy Rule establishes the floor for protected health information protection. If similar state laws are contrary to the provisions of HIPAA—that is, if it is impossible to comply with both state and Federal laws or the state law presents obstacles to the compliance of Federal laws, HIPAA preempts similar state laws. If state

[46] Medical surveillance refers "the analysis of health information to look for problems that may be occurring in the workplace that require targeted prevention. Thus, surveillance serves as a feedback loop to the employer. Surveillance may be based on a single case or sentinel event, but more typically uses screening results from the group of employees being evaluated to look for abnormal trends in health status." (OSHA: https://www.osha.gov/SLTC/medicalsurveillance/surveillance.html; accessed November 15, 2020). Examples of medical surveillance may include tests for exposures to hazardous materials such as radiation sources, asbestos, and cyanide (https://www.osha.gov/Publications/complinks/OSHG-HazWaste/5-6.pdf; accessed November 15, 2020).

laws afford greater protection of protected health information than does HIPAA, then state laws prevail.

5.2.3 Interface between HIPAA and ADA

Although the provisions of HIPAA and ADA generally affect different areas of employment, they interface under limited circumstances. Therefore, it is important to understand when they interface, and when the related compliance requirements are applicable in the workplace.

One of the interfacing points of the ADA and HIPAA is the reasonable accommodation process. When an employee with a disability requests reasonable accommodation, the employer and the employee will engage in an interactive process to understand the nature of the employee's request and to determine what reasonable accommodation is appropriate. If the information about the disability and the requested accommodation is unclear or insufficient, the employer is not prohibited by the ADA from asking for additional information related to the employee's disability to make a determination regarding reasonable accommodation (i.e., without undue burden on the employer). To that end, the employer may ask the employee to provide documentation related to his/her disability. In this case, the employee can provide to the employer medical records pertaining to the disability. Also, the employer is not prohibited by HIPAA from directly contacting the employee's healthcare provider(s) to request additional information (e.g., medical record, prescriptions, etc.) about the employee's disability for which reasonable accommodation is requested. The healthcare provider can, however, disclose protected health information to the employer only if the employee has given the health provider HIPAA-compliant authorization to release such information to the employer and the extent of the disclosure is limited only to the information associated with the disability for which reasonable accommodation is sought. That is, if the individual has multiple disabilities, medical information regarding disabilities not associated with the reasonable accommodation request cannot be disclosed by the healthcare provider to the employer.

Also, if an employer sponsors a group health plan for its employees, even if the employer is not a covered entity, the group health plan itself is a covered entity under HIPAA and the plan is required to ensure individual employee's health information is protected, kept confidential, and will not be released without the employee's HIPAA-compliant authorization. Even if the employer is not a HIPAA-covered entity, as mentioned in Section 5.1.4, it is not required to comply with HIPAA Privacy and Security Rules, but it is required by ADA to keep employees' medical information associated with disability-based inquiries and information confidential and separate from employment records.

5.2.4 Implications for Fitness for Duty

Whether or not and to what extent a licensee or other entity is subject to HIPAA-compliance requirements depends on whether it is a HIPAA-covered entity or business associate, the nature of the personal information obtained from individuals, and how such information is handled. The types of activities performed as part of FFD programs by the licensees and other entities include those that are non-healthcare-related, such as workplace drug testing and fitness determination, which are conducted in compliance with NRC FFD regulations, as well as those that meet the definition of healthcare in HIPAA (45 CFR 160.103), such as substance abuse treatment programs administered by an SAE.

10 CFR 26.37 and 26.411 require licensees and other entities protect individuals' privacy by establishing, using, and maintaining a system of files and procedures to keep drug-testing results

confidential and require signed consent before personal information collected and maintained under the FFD program can be disclosed except for specific circumstances (§ 27.37(b)). For FFD-related activities that trigger HIPAA protection, the involved parties (e.g., SAEs, clinics) are required to also comply with HIPAA Privacy and Security Rules. The 2019 NRC Inspection Manual illustrates the importance of SAEs to maintain electronic and paper records in accordance with HIPAA requirements as well as those of the NRC regulations (NRC 2019).

When making disability-related inquires, e.g., requesting medical records or prescription information, from individuals requesting reasonable accommodation and/or from HIPAA-covered entities such as healthcare providers, licensees and entities should be aware that HIPAA-compliant authorization should be in place before such information can be disclosed.

Drug-testing laboratories or clinics that are covered entities or business associates must obtain HIPAA-compliant authorization from individual donors before disclosing testing results to their employers. However, it is worth pointing out the Privacy Rule does not prohibit employers from making an individual providing authorization for information disclosure a condition of employment (HHS 2002).

5.3 Family and Medical Leave Act

The Family and Medical Leave Act of 1993 (hereafter, FMLA) protects the rights of employees to take unpaid leave for up to 12 workweeks during any 12-month period for reasons such as childbirth and newborn childcare, adoption and related child care, serious health conditions, caring for the employee's family, and active military duty; or 26 workweeks of military caregiver leave in a single 12-month period for an eligible employee who is a family member of a covered servicemember needing care for a serious injury or illness (Department of Labor [DOL] n.d.).

Individuals must meet the qualifying conditions to become eligible for FMLA protection. Among the qualifying conditions defined in FMLA, the term "serious health condition" warrants elaboration. FMLA defines serious health conditions as "an illness, injury, impairment, or physical or mental condition that involves inpatient care in a hospital or facility or continuing treatment by a health care provider" (FMLA Section 101(11)).

Based on this definition, 29 CFR 825.113 (C) stipulates that conditions that are short in duration and have limited impact on individuals' capacity, such as the flu, colds, upset stomach, and (non-migraine) headaches, are not considered serious conditions. In a DOL opinion letter (DOL 1996), the DOL acknowledges that while it is straightforward to establish that absence due to inpatient care qualifies as a serious health condition, whether "continuing treatment by a health care provider" constitutes a serious health condition requires further examination of the regulation. Section 825.114(a)(2)(i) sets the three-day incapacity rule as the benchmark for establishing continuing treatment as a serious health condition. Continuing treatment by a healthcare provider is considered a serious condition if the condition results in more than three consecutive calendar days of incapacity and any subsequence treatment or continued incapacity, and requires the following:

- Treatment two or more times by a health care provider, by a nurse or physician's assistant under direct supervision of a health care provider, or by a provider of health care services (e.g., physical therapist) under orders of, or on referral by, a health care provider; or

- Treatment by a health care provider on at least one occasion which results in a regimen of continuing treatment under the supervision of the health care provider (§ 825.114(b)).

The regulation further clarifies that a regimen of continuing treatment could include a course of prescription medication (e.g., an antibiotic) but it does not include treatment that does not involve a visit to a healthcare provider. Treatment such as taking over-the-counter medication and bed rest is not considered a regimen of continuing treatment under FMLA and does not trigger FMLA protection.

In the workplace, the employee requesting FMLA leave bears the responsibility of providing a complete and sufficient medical certification or necessary authorization to allow the employee's healthcare provider to release such certification, upon the request by the employer (§ 825.305). If the validity of the initial certification is challenged, the employer can require the employee to obtain a second opinion from a different healthcare provider at the employer's expense. In case of additional challenge of the second opinion, a final and binding third opinion shall be obtained at the employer's cost and with the mutual agreement of the employer and the employee (§ 825.307). If the medical certification fails to meet FMLA requirements, the employer can deny the employee's FMLA leave request.

5.4 Occupational Safety and Health Administration

To protect worker safety and health, OSHA, an agency of the DOL, has established standards for recording and reporting occupational injuries and illnesses (29 CFR 1904). With the exception of partial exemptions stipulated in §§ 1904.1 and 2 (e.g., employers with no more than 10 employees or employers in certain industries), employers are required to keep accurate and timely records of work-related injuries and illnesses, including fatalities, injuries, and illnesses that meet the general recording criteria in § 1904.7 or specific cases in §§ 1904.8-12. The general recording criteria require that employers record injury or illness that result in fatalities, work absence, work restriction or job transfer, medical treatment beyond first aid, the loss of consciousness, and any such significant injuries or illnesses diagnosed by a licensed healthcare professional. OSHA's Form 300, Log of Work-Related Injuries and Illnesses, is used by employers to document all recordable injuries and illnesses of all employees on the employer's payroll.[47] Employers are required to report work-related fatalities within 8 hours of the incident and work-related inpatient hospitalization, amputation, or loss of an eye within 24 hours by phone, in person, or through the OSHA web portal.

OSHA has provided clarification in its regulation to address issues related to implementing the recording and reporting requirements. Among them, the issues regarding work restriction and job transfer, and workplace drug testing are of particular relevance to this report.

Employees are required to record work restrictions and job transfers resulting from work-related injuries or illnesses. The determination of whether an injury or illness caused work restriction should be based on whether the employee can perform his/her routine functions (i.e., work activities regularly performed by an employee at least once per week) in the context of his/her job or if he/she can work full-time as otherwise typically scheduled, or by recommendation from a licensed healthcare professional. Similarly, if a work-related injury or illness resulted in the employee being assigned to a job other than his/her regular job, such job transfer is a recordable event and the employee must record it accordingly. Work restriction or job transfer limited to the

[47] See OSHA's Form 300 at https://www.osha.gov/recordkeeping/new-osha300form1-1-04-FormsOnly.pdf.

day of the injury or illness is not recordable. In case the work restriction recommendation from licensed healthcare professionals is unclear, the employer may ask the recommending physician (1) whether the employee can perform all his/her routine job functions; and (2) whether the employee can work all his/her regular work shift. If the answer to either of the questions is no, then the employee must record it as an OSHA work restriction. As mentioned in Section 5.2.1, the information request from an employer to a licensed healthcare professional regarding OSHA recordable and reportable injuries and illnesses is in compliance with the OSHA regulation and is not subject to the HIPAA Privacy Rule (45 CFR 164.512(a) and (b)). Thus, no employee authorization is required prior to information disclosure to the employer. It is important to note that OSHA does not prohibit employers from conducting drug tests on employees reporting work-related injuries or illnesses if the employer has an objective reason for doing so (29 CFR 1904.35(b)). Under the current OSHA regulation, an individual can be drug tested to determine if he/she was impaired at the time of the reportable injury or illness and the permissible impairment testing is limited to alcohol testing, as OSHA clarifies in a 2016 memorandum:

> OSHA will consider whether the drug test is capable of measuring impairment at the time the injury or illness occurred where such a test is available. Therefore, at this time, OSHA may consider this factor for tests that measure alcohol use, but not for tests that measure the use of any other drugs (Cordaro 2016; OSHA 2016 and 2018).

To stay compliant, employers should ensure post-accident drug and alcohol testing is consistent with the OSHA regulation. Employers are also required to establish a reasonable reporting procedure. OSHA deems a procedure unreasonable if it has a deterring or dampening effect on a reasonable employee regarding workplace injury or illness reporting. Further, OSHA offers protection of employees who report work-related injuries or illnesses against employer's retaliation (§ 1904.35(b)(1)(iv)). Employees must not be discharged or discriminated against by employers for reporting workplace injuries or illnesses.

5.5 Additional Considerations

In addition to the ADA, HIPAA, and OSHA, Federal and state laws have established further requirements regarding prescription drug dispensing, refills, and supply to prevent fraud and drug abuse (Blake 2013). As discussed in Section 2.4.5, many states have established prescription monitoring programs, many of which are known as PMDPs (CDC 2019), to collect and store information about dispensing prescription medication and controlled substances. At the Federal level, the National All Schedules Prescription Electronic Reporting Act of 2005 established HHS grant programs to provide implementation and enhancement support of the PMDPs.

Further, DEA and many state laws set limits on the supply, prescribing, dispensing, and refilling of certain prescription medication and controlled substances (CDC 2015). Across the states, permitted days of supplies for different schedules of prescription medication may vary. For example, Missouri state law requires that the supply of Schedule II drugs is limited to 30 days and that of Schedule III, IV, and V drugs is limited to 90 days. South Carolina state law limits the supply of Schedule III, IV, and V drugs to 30 days. In California, Schedule II drug supplies are subject to a 72-hour limit. Some state laws have placed similar restrictions on refilling certain prescription medication and controlled substances. The California Health & Safety Code stipulates that Schedule II substances may not be refilled, Schedule III or IV controlled substance can be refilled no more than five times, and the total refills of these substances cannot exceed 120 days of total supply (Health & Safety Code Section 11200 (b)). In Washington State, the state law requires that Schedule II substances may not be refilled and the refills of Schedule III, IV, or V

substances shall be limited to no more than five times (RCW 69.50.308). Some state laws specify the dosage limits on certain prescription medications or controlled substances. For example, Rhode Island state law explicitly defines the quantity of a dosage unit and sets the prescribing and one-time dispensing dosage limit of Schedule III substances to no more than 100 units and the dispensing dosage limit for Schedules IV and V substances is 360 units at one time (Rhode Island General Laws 21-28-3.18). Arkansas state law specifies that although Schedule V substances that are not prescription drugs can be dispensed by pharmacists at retail, the dispensing dosage shall not exceed 24 dosage units if such substances contain opium, or 24 dosage units if they contain other such controlled substances, in any given 48-hour period (Arkansas Administrative Code 070.00.7-07-04-0007).

Similarly, state laws also target and sanction fraudulent practices (e.g., deceit, doctor shopping, drug diversion) in obtaining prescription drugs and/or controlled substances. In particular, doctor shopping—obtaining prescription/controlled substances from multiple practitioners without the practitioners' knowledge that the prescription is being sought from other practitioners as well—is regulated by general doctor shopping laws in most states and/or specific doctor shopping laws in some states (CDC n.d.). Most states have promulgated general doctor shopping laws that leverage the stipulations from the Uniform Narcotic Drug Act of 1932 and/or the Uniform Controlled Substances Act of 1970 to make it illegal to obtain prescription drugs and/or controlled substances through "fraud, deceit, misrepresentation, subterfuge, or concealment of material fact" (Uniform Narcotic Drug Act of 1932). Specific doctor shopping laws make it unlawful for a patient to knowingly or purposefully withhold information from a practitioner that the prescription medication or controlled substance or similar substance(s) being sought has already been prescribed by another practitioner or other practitioners. The specific doctor shopping laws may set specific requirements regarding the patients' disclosure time frame, types of drugs, and disclosure requirements. For example, Montana and Wyoming state laws require patients to disclose prescriptions for the same or similar controlled substances within 30 days, while in Connecticut (Connecticut General Statute Section 21a-266) and Georgia (Georgia Code Section 16-13-43) disclosure is required for the concurrent time period. The state of Louisiana requires patients to disclose, in writing, details regarding the name of the controlled substance, prescription date, amount and the number of refills, and the disclosure shall be part of the patients' medical records (Louisiana Revised Statutes Section 40:971). In addition, many states' doctor shopping laws specify that patient-practitioner communication for the purpose of unlawfully obtaining drugs is not deemed privileged communication and is not protected as such.

Finally, Federal and state laws also have provisions criminalizing illegal prescription use, possession and trafficking. The CSA specifies that Schedule II, III, and IV substances that are prescription drugs may not be dispensed without a written or oral prescription in conformance with Section 503(b) of the CSA [21 U.S.C. 353(b)]. In all states, possessing and trafficking controlled substance without a prescription is unlawful as is stealing others' prescriptions and unauthorized possession of prescription pads, blanks, and forms with the intent to obtain and/or distribute such substances (NAMSDL 2009). For example, Utah State Statute Section 58-17b-501 defines "unlawful conduct" to include the following:

> (11) selling, dispensing, or otherwise trafficking in prescription drugs when not licensed to do so or when not exempted from licensure; and
>
> (12) a person using a prescription drug or controlled substance that was not lawfully prescribed for the person by a practitioner.

A recent Florida case involving drug trafficking illustrates the importance of clearly understanding the Federal and state laws related to these issues. In this case, the defendant, wife of a patient,

was arrested and charged with drug trafficking when her husband's oxycodone, which was kept in an unlabeled vial, was found in her vehicle by police during investigation of a traffic offense. The defendant reported to have routinely held and transported her husband's medication as the husband's work attire did not have any pockets and the husband used the medication regularly to manage his chronic backpain. The trial court decided the defendant was guilty of drug trafficking but the state's court of appeals eventually exonerated the defendant on the ground that the trial court failed to tell the defendant about the "prescription defense" doctrine[48] and thus erred in failing to give the defendant a fair trial (Vivian 2011). As rare as it may be, the case demonstrates that to stay within the boundary of law, knowledge and due diligence is required when individuals obtain, use, possess, dispense, and transport prescription medication and controlled substances.

5.5 Implications for Fitness for Duty

The legal protection afforded by ADA and FMLA, the compliance requirements of the HIPAA and OSHA, and the provisions of the various Federal and state laws regarding prescription medication and controlled substances dispensing, refills, possession, and trafficking collectively create a complex legal and policy environment in which prescription drug use in the workplace is managed to ensure the effectiveness of the FFD program. Licensees and other entities and individuals subject to Part 26 have shared responsibilities to ensure the workplace is free from the influence of drugs, prescription or otherwise.

The NRC's FFD rule requires that individuals subject to Part 26 be trustworthy and reliable. To demonstrate trustworthiness and reliability regarding prescription drug use in the workplace, such individuals need to follow instructions from treating physicians/healthcare professionals and use medications in the manner prescribed so that they can remain fit for duty and competently perform their job duties. These individuals also need to recognize and adhere to the legal requirements associated with obtaining, administering, and refilling prescription medications and avoid any deceit, fraud, misrepresentation in prescription medication procurement and use. To be fit for duty also means such individuals need to do their due diligence in support of the FFD program, reporting impairment affecting their job performance as appropriate and reporting any reasonable suspicion involving others' drug abuse, addiction, and performance impairment in the workplace.

For the licensees and entities regulated by the NRC, it is important to understand and uphold the legal rights and employment protection afforded to the individuals performing work at these entities' facilities. In implementing FFD programs, the licensees and entities need to be aware of their compliance responsibilities and understand the interface and interplay among such agencies as FFD, ADA, HIPAA, and OSHA in making disability-based inquiries, determining reasonable accommodations, obtaining individuals' protected health information, reporting work-related incidents, and conducting drug tests and fitness determinations. While licensees and other entities have the legal obligation to ensure employee fitness for duty by conducting drug testing and certain medical inquiries or assessments, it is important that such assessments be work-related, individualized, and based on real risk to the workplace and business necessity. In addition, it is noteworthy that although some licensees have established company policy for self-reporting prescription drug use that might affect individuals' ability to perform the essential job functions,

[48] The prescription defense doctrine is based on Florida statute 893.13(1)(h)(6)(a), which states, "It is unlawful for any person to be in actual or constructive possession of a controlled substance unless such controlled substance was lawfully obtained from a practitioner or pursuant to a valid prescription or order of a practitioner while acting in the course of his or her professional practice or to be in actual or constructive possession of a controlled substance except as otherwise authorized by this chapter. Any person who violates this provision commits a felony of the third degree."

such policy is not currently mandated by 10 CFR Part 26. Results of the recent litigation suggest that a blanket prescription reporting policy—requiring all employees to self-report all prescription drug use—is not recommended because it is likely to reveal individuals' underlying medical conditions that the individuals might not wish to disclose, thereby running the risk of violating the ADA's employment provisions.

In summary, understanding the complex legal and compliance requirements in implementing FFD programs will help licensees and other entities subject to Part 26 strike a balance between ensuring fitness for duty and protecting public health and safety and protecting individuals' rights to privacy and employment protection from discrimination on the basis of disabilities.

6.0 Conclusions on Workplace Prescription Drug Use

With the growing prevalence of prescription drug use, identifying and managing the impacts of prescription drug impairment in the workplace, especially for positions that involve performing safety- and security-sensitive functions, are of great importance for individual workers' health and safety and that of the public.

The review of prescription medication suggests that despite the growing number of prescription drugs available in the U.S. and the advances in medical and pharmacological research, it remains a challenge to precisely and reliably predict the side effects likely to be experienced by drug takers due to variations in individual characteristics such as age, gender, weight, genetic predisposition, existing physical conditions, metabolism, drug tolerance, drug interaction, and lifestyle. An added complexity of the issue regarding prescription medication use in the workplace is the difficulty in leveraging prescription medications' therapeutic and side effects to reliably estimate the duration and severity of impairment effects on individuals performing their job duties. The challenge in linking medication use to impairment is twofold. First, the likely side effects of taking prescription medication can vary wildly from one individual to another. The same medication could have negligible side effects for some but debilitating effects for others. Second, whether an individual's drug effects amount to impairment cannot be meaningfully established without considering defined metrics associated with specific job duties and work environments. It is important to recognize, for instance, a medication that might cause dizziness could mean work restriction for operators who might climb ladders, but it might not affect a desk worker to the extent that work restriction is necessary. Therefore, a meaningful impairment determination requires an individualized assessment in the context of an individual's physical condition, specific job duties, and, if available, performance measured against an established performance standard.

The NRC FFD program's regulatory framework provides flexible tools to ensure the workforce is fit for duty by managing for possible impacts due to covered individuals' prescription drug use. Self-reporting and behavioral observation serve to identify drug effects that give rise to potential impairment in the workplace. The FFD rule specifies the procedures, processes, roles and responsibilities, and personnel qualifications for making fitness determinations. The rule also stipulates policy violations and sanctions for prescription medication misuse and abuse based on determination by qualified professionals such as the MRO and/or SAE. Within a licensee's FFD program, the rule offers flexibility for licensees and other entities to pursue additional measures to ensure employee fitness for duty. Such measures could include expanding the drug-testing panel with other DEA-scheduled drugs, determining specific sanctions for misuse, and imposing greater-than-minimum sanctions in response to policy violations.

A survey of the prescription drug policies, requirements, and guidance implemented by other Federal agencies suggests a lack of uniformity in their policy approaches. Some agencies (e.g., FAA) have issued more defined and restrictive guidance for prescription medication use in the workplace and have used accident statistics to inform the guidance regarding drugs that have impairing effects on certain segment(s) of the workforce (e.g., flight crew). Some agencies have invested in public campaigns to educate the workforce in safety- and security-sensitive industries and to raise their awareness of the impacts of prescription medications on the workplace and how they might affect public health and safety. This information can be complementary to FFD programs. The FFD rule does not explicitly prohibit the use of specific prescription medications and it gives licensees and other entities the discretion to establish company policies such as those addressing self-reporting and restrictions on certain prescription medications to meet their specific organizational needs. The knowledge, insight, and lessons learned from these other

Federal agencies can help inform licensees when developing more targeted and effective prescription drug policy that suits their operations and management structure.

The legal protection for individuals afforded by ADA and FMLA, the compliance requirements of HIPAA and OSHA, and the provisions of the FDA and various other Federal and state laws for prescription medication and controlled substance approval, dispensing, refills, possession, use, and trafficking collectively create a complex legal and policy environment in which FFD concerns for workplace prescription drug use must be managed. Similar to fitness determinations, the ADA requires that employers make individualized assessments regarding the employee's ability to perform the essential job functions of positions the individual desires or holds. To comply with these policies and the FFD requirements, licensees and other entities and individuals subject to Part 26 have shared responsibilities to ensure that the individuals are fit for duty, reliable, and trustworthy, and that the workplace is free from the influence of drugs, prescription or otherwise, while these individual's rights are duly protected.

In conclusion, understanding the technical complexity associated with prescription medication, their varied side effects, and potential impairing effects on individuals in the context of their job duties is an important component of an effective FFD program. Similarly, recognizing the limitations of the current workplace drug-testing practices and the legal and compliance requirements in implementing FFD programs will help licensees and other entities subject to Part 26 strike a balance between ensuring employee fitness for duty and protecting public health and safety and upholding the legal protection involving employment practices, protected health information, and worker safety. As the need to better manage prescription drug use in the workplace increases, additional considerations such as using data-driven approaches to establish linkages between accidents/incidents and prescription medication use, and exploring the feasibility of implementing prevalence testing while understanding the legal boundaries and implications for individual protection, would contribute to greater effectiveness of the FFD programs of licensees and other entities.

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Appendix A – Prescription Drug Use Data

Data presented in this appendix are collected by the Centers for Disease Control and Prevention and reported in *Health, United States,* which presents the health status of the country each year. The report presents an overview of national health trends organized around four subject areas: health status and determinants, utilization of health resources, healthcare resources, and healthcare expenditures and payers. The report is submitted by the Secretary of the U.S. Department of Health and Human Services to the President and the Congress of the United States. The full report is available at: https://www.cdc.gov/nchs/hus/description.htm.

Table A-1. Prescription drug use by a percent of the population in the past 30 days by sex and age.

Sex and age cohort	At least one prescription drug in past 30 days								Three or more prescription drugs in past 30 days								Five or more prescription drugs in past 30 days							
	1988–1994	1999–2002	2001–2004	2003–2006	2005–2008	2007–2010	2009–2012	2011–2014	1988–1994	1999–2002	2001–2004	2003–2006	2005–2008	2007–2010	2009–2012	2011–2014	1988–1994	1999–2002	2001–2004	2003–2006	2005–2008	2007–2010	2009–2012	2011–2014
All ages, age-adjusted[b]																								
Both sexes[c]	39.1	45.2	46.7	46.9	47.2	47.5	47.3	46.9	11.8	17.8	20.2	21.0	20.8	20.8	20.6	21.5	4.0	7.5	9.2	10.0	10.2	10.1	10.1	10.9
Male	32.7	39.8	41.6	41.7	41.8	42.8	42.7	42.6	9.4	14.8	17.3	18.0	18.3	19.1	19.1	19.7	2.9	6.1	7.9	8.4	8.9	9.2	9.3	9.7
Female	45.0	50.3	51.5	51.9	52.4	52.0	51.8	51.2	13.9	20.4	22.8	23.8	23.2	22.5	22.0	23.2	4.9	8.7	10.4	11.4	11.5	11.0	10.8	12.0
All ages, crude																								
Both sexes[c]	37.8	45.0	46.5	47.3	47.9	48.5	48.7	48.9	11.0	17.6	19.9	21.3	21.4	21.7	21.8	23.1	3.6	7.4	9.0	10.1	10.5	10.6	10.7	11.9
Male	30.6	38.6	40.5	41.1	41.7	43.0	43.4	43.7	8.3	13.9	16.4	17.4	17.8	19.0	19.4	20.4	2.5	5.6	7.3	8.0	8.6	9.1	9.3	10.0
Female	44.6	51.1	52.2	53.2	53.9	53.8	53.9	53.9	13.6	21.1	23.4	25.1	24.8	24.2	24.1	25.8	4.7	9.1	10.7	12.2	12.4	12.1	12.0	13.6
Both sexes																								
Under 18 years	20.5	23.8	23.9	24.7	25.3	24.0	23.5	21.5	2.4	4.1	4.0	4.0	4.4	3.8	3.6	3.9	*	*0.8	0.8	*0.9	1.0	0.8	0.8	0.8
18–44 years	31.3	35.9	37.7	37.4	37.8	38.7	38.1	37.1	5.7	8.4	10.2	10.6	9.8	9.7	9.6	10.1	1.2	2.3	3.3	3.5	3.4	3.1	3.3	3.9
45–64 years	54.8	64.1	66.2	65.2	64.8	66.2	67.2	69.0	20.0	30.8	34.2	35.3	34.1	34.4	34.7	36.4	7.4	13.3	15.7	17.1	17.0	16.8	16.3	18.3
65 years and over	73.6	84.7	87.3	89.4	90.1	89.7	89.8	90.6	35.3	51.8	59.8	62.9	65.0	66.6	64.8	66.8	13.8	27.1	33.3	36.1	38.3	39.7	39.1	40.7
Male																								
Under 18 years	20.4	25.7	25.3	25.3	25.3	24.5	23.1	21.1	2.6	4.3	4.1	4.0	5.0	4.4	4.1	4.3	*	*	*0.8	*1.0	*1.1	0.8	0.9	0.9
18–44 years	21.5	27.1	29.2	28.0	27.5	29.5	29.6	28.8	3.6	6.7	8.0	6.9	6.2	7.1	7.5	7.5	*0.8	1.7	2.6	2.1	*1.8	2.1	2.8	3.0
45–64 years	47.2	55.6	58.7	58.4	59.3	61.3	63.1	65.6	15.1	23.6	28.3	29.8	28.6	30.4	31.4	33.0	4.8	9.5	12.5	13.4	13.7	14.4	14.2	15.7
65 years and over	67.2	80.1	83.6	88.2	89.7	88.8	87.7	88.7	31.3	46.3	54.2	60.5	64.6	66.8	64.6	65.2	11.3	24.7	30.6	34.5	38.4	39.5	37.9	38.4
Female																								
Under 18 years	20.6	21.7	22.4	24.0	25.2	23.5	23.8	22.0	2.3	3.9	3.9	4.0	3.8	3.1	3.1	3.5	*	*0.8	*0.7	*0.7	*0.8	*0.7	*0.6	*
18–44 years	40.7	44.6	45.9	46.6	47.9	47.6	46.4	45.3	7.6	10.2	12.3	14.3	13.3	12.2	11.8	12.6	1.7	2.8	3.9	4.9	5.0	4.0	3.9	4.8
45–64 years	62.0	72.0	73.4	71.6	70.2	70.8	71.1	72.1	24.7	37.5	39.9	40.6	39.4	38.1	37.8	39.4	9.7	16.8	18.8	20.7	20.2	19.1	18.3	20.7
65 years and over	78.3	88.1	90.1	90.3	90.5	90.4	91.4	92.1	38.2	55.9	64.0	64.7	65.3	66.4	64.9	68.1	15.6	28.9	35.4	37.4	38.3	39.8	40.0	42.6

- - - Data not available.

* Estimates are considered unreliable. Data preceded by an asterisk have a relative standard error (RSE) of 20%–30%. Data not shown have an RSE greater than 30%.

[a] Estimates are age-adjusted to the year 2000 standard population using four age groups: under 18 years, 18–44 years, 45–64 years, and 65 years and over. Age-adjusted estimates in this table may differ from other age-adjusted estimates based on the same data and presented elsewhere if different age groups are used in the adjustment procedure. See Appendix II, Age adjustment.

[b] Includes persons of all races and Hispanic origins, not just those shown separately.

NOTES: See *Health, United States,* Appendix II, Drug. Standard errors are available in the spreadsheet version of this table. Data for additional years are available. See the Excel spreadsheet on the *Health, United States* website at: https://www.cdc.gov/nchs/hus.htm.

Table A-2. Prescription drug therapeutic class usage trends for working age adults.

Age group and Multum Lexicon Plus therapeutic class[a1] (common indications for use)	Total				Male				Female			
	1988–1994	1999–2002	2007–2010	2011–2014	1988–1994	1999–2002	2007–2010	2011–2014	1988–1994	1999–2002	2007–2010	2011–2014
18–44 years												
Analgesics (pain relief)	7.2	8.0	8.0	7.0	5.1	6.0	6.6	5.3	9.1	9.9	9.3	8.8
Antidepressants (depression and related disorders)	1.6	6.0	7.9	8.8	*1.0	3.6	4.4	6.4	2.3	8.5	11.3	11.2
Sex hormones (contraceptives, menopause, hot flashes)[b]	...	...	...	...	...	...	...	...	11.5	13.5	15.5	13.4
Proton pump inhibitors or H2 antagonists (gastric reflux, ulcers)[c]	2.0	3.0	5.0	3.8	1.6	3.0	4.5	4.2	2.4	3.0	5.5	3.4
Anxiolytics, sedatives, and hypnotics (anxiety, insomnia, and related disorders)	1.4	2.1	3.8	4.2	*1.0	*1.7	3.0	3.5	1.9	2.5	4.7	5.0
Anticonvulsants (epilepsy, seizure, and related disorders)	0.8	1.6	3.3	4.1	*0.6	1.6	2.7	4.0	1.0	*1.5	3.9	4.2
Bronchodilators (asthma, breathing)	1.4	2.2	3.2	2.9	*1.1	1.6	2.2	2.6	*1.8	2.8	4.3	3.2
Antihyperlipidemic agents (high cholesterol)	*0.4	1.3	2.8	2.3	*	2.0	3.3	2.9	*	*	2.3	1.8
Antihistamines (allergies)	2.5	3.9	2.5	1.8	1.8	3.6	*1.7	*1.6	3.2	4.2	3.3	*2.0
Thyroid hormones (hypothyroidism)	1.3	1.6	2.3	2.2	*	*	*	*0.7	2.1	2.8	4.2	3.6
ACE inhibitors (high blood pressure, heart disease)	0.7	1.4	2.0	2.1	*0.9	1.5	2.1	2.1	*0.6	*1.2	1.9	2.2
Antidiabetic agents (diabetes)	*1.0	1.5	1.9	2.5	*	*1.5	1.7	2.1	*1.0	*1.6	2.2	2.9
Muscle relaxants (muscle spasm and related disorders)	1.0	1.3	1.6	1.7	*1.3	*1.1	*1.4	1.4	*0.7	*1.4	1.9	2.1
Beta-adrenergic blocking agents (high blood pressure, heart disease)	1.1	*1.2	1.6	1.6	*0.9	*1.3	1.3	1.2	1.3	*	1.8	2.0
Nasal preparations (nose symptoms)	*0.6	1.5	1.6	1.4	*	*1.2	*1.3	*0.8	*0.7	1.7	1.8	2.1
45–64 years												
Antihyperlipidemic agents (high cholesterol)	4.3	13.8	21.9	25.6	4.4	17.2	24.7	28.2	4.2	10.7	19.2	23.1
Proton pump inhibitors or H2 antagonists (gastric reflux, ulcers)[c]	5.2	9.9	14.8	14.1	5.3	8.4	13.8	12.7	5.2	11.3	15.6	15.4
Antidepressants (depression and related disorders)	3.5	10.5	14.4	17.5	*2.3	7.0	8.9	12.5	4.6	13.8	19.6	22.2
Sex hormones (contraceptives, menopause, hot flashes)[b]	...	...	...	...	...	...	...	...	19.9	30.3	8.1	10.1
Analgesics (pain relief)	11.9	16.0	14.1	15.5	9.2	13.5	12.5	14.3	14.3	18.3	15.6	16.7
Beta-adrenergic blocking agents (high blood pressure, heart disease)	6.6	8.7	11.1	11.5	7.0	7.8	11.3	10.8	6.2	9.5	10.9	12.1
ACE inhibitors (high blood pressure, heart disease)	5.2	8.8	11.0	12.5	5.7	9.8	12.4	14.9	4.6	7.9	9.8	10.2
Antidiabetic agents (diabetes)	5.5	7.0	10.1	11.3	5.9	7.8	10.7	12.5	5.1	6.3	9.5	10.2
Thyroid hormones (hypothyroidism)	4.7	6.6	8.5	8.1	*1.2	*2.7	3.5	*2.6	8.1	10.1	13.2	13.2
Antihypertensive combinations (high blood pressure)	5.3	5.6	8.4	7.9	3.3	*3.7	7.9	7.4	7.1	7.3	8.9	8.3
Anxiolytics, sedatives, and hypnotics (anxiety, insomnia, and related disorders)	6.0	6.2	7.9	8.6	4.3	4.9	6.9	7.7	7.5	7.4	9.0	9.4
Diuretics (high blood pressure, heart disease, kidney disease)[d]	6.1	6.6	7.2	8.6	4.8	4.8	5.8	7.2	7.3	8.3	8.5	9.9
Anticonvulsants (epilepsy, seizure, and related disorders)	2.7	4.3	6.4	7.5	*2.5	3.5	5.6	6.3	2.9	5.1	7.1	8.6
Bronchodilators (asthma, breathing)	3.4	3.8	6.1	5.2	2.9	3.1	5.0	*4.6	3.8	4.5	7.2	5.8
Calcium channel blocking agents (high blood pressure, heart disease)	7.0	6.7	5.4	6.6	8.2	5.9	5.4	7.9	5.9	7.5	5.4	5.4

... Category not applicable.

* Estimates are considered unreliable. Data preceded by an asterisk have a relative standard error (RSE) of 20%–30%. Data not shown have an RSE greater than 30%.

[a] The drug therapeutic class is based on the December 2014 Lexicon Plus, a proprietary database of Cerner Multum, Inc. Lexicon Plus is a comprehensive database of all prescription and some nonprescription drug products available in the U.S. drug market. Data was collected by the National Health and Nutrition Examination Survey. Respondents were asked if they had taken a prescription drug in the past 30 days. Those who answered "yes" were asked to show the interviewer the medication containers for all prescriptions. If no container was available, the respondent was asked to verbally report the name of the medication. Each drug's complete name was recorded and classified. Data presented here are based on the second-level classification of prescription drugs. Up to four classes are assigned to each drug. Drugs classified into more than one class were counted in each class. For more information, see https://wwwn.cdc.gov/nchs/nhanes/1999-2000/RXQ_DRUG.htm. See Appendix II of the Health, United States report, Multum Lexicon Plus therapeutic class.

[b] Although sex hormones may be used by males, most are used by females. Therefore, data for sex hormones are only presented for females.

[c] The drugs classes proton pump inhibitors (272) and H2 antagonists (94) have been combined because of their similar indications for use.

[d] This category includes carbonic anhydrase inhibitors that are primarily used to treat glaucoma.

NOTES: Some drug classes were not available in 1988–1994 and are coded as not applicable. See *Health, United States,* Appendix II, Drug. Standard errors are available in the spreadsheet version of this table. Available from: https://www.cdc.gov/nchs/hus.htm.

Appendix B – Regulation of Prescription Drugs

This appendix provides a high-level overview of the U.S. Department of Health and Human Services (HHS), U.S. Department of Justice (DOJ), and United States Pharmacopeia (USP) missions and their roles in the regulatory framework for ensuring safe and well-regulated prescription drug use.

B.1 Department of Health and Human Services

Within the HHS, the following agencies and offices regulate various aspects of prescription drug marketing, use, and control in the United States:

- FDA – The Food and Drug Administration, part of the Public Health Service, ensures that food is safe, pure, and wholesome; human and animal drugs, biological products, and medical devices are safe and effective; and electronic products that emit radiation are safe. In particular, FDA is responsible for approving drug products, maintaining lists of drug products, and establishing mandated drug labeling information. In addition to authorities under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act requires manufacturers of biologic products to hold an FDA-issued license for these products.
- SAMHSA – The Substance Abuse and Mental Health Services Administration, part of the Public Health Service, improves access and reduces barriers to high-quality, effective programs and services for individuals who suffer from or are at risk for addictive and mental disorders, as well as for their families and communities. An explicit part of SAMHSA's mission is "… to reduce the impact of substance abuse … on America's communities."
- CDC – The Centers for Disease Control and Prevention, part of the Public Health Service, protects the public health of the nation by providing leadership and direction in the prevention and control of diseases and other preventable conditions, and responding to public health emergencies. Prescription drug-use rates are among the statistics tracked by the CDC.
- CMS – The Centers for Medicare & Medicaid Services combines the oversight of the Medicare program, the federal portion of the Medicaid program and State Children's Health Insurance Program, the Health Insurance Marketplace, and related quality assurance activities. Medicare requires each insurer's covered drug list (formulary) to include at least two drugs in the most commonly prescribed categories and classes.
- NIH – The National Institutes of Health, part of the Public Health Service, supports biomedical and behavioral research in the United States and abroad, conducts research in its own laboratories and clinics, trains promising young researchers, and promotes collecting and sharing medical knowledge. NIH's organization includes the National Institute on Drug Abuse (NIDA), a part of the U.S. Public Health Service, and the National Library of Medicine (NLM):
  - NIDA's mission is to advance science on the causes and consequences of drug use and addiction and to apply that knowledge to improve individual and public health. This involves (1) strategically supporting and conducting basic and clinical research on drug use, its consequences, and the underlying neurobiological, behavioral, and social mechanisms involved, and (2) ensuring the effective translation, implementation, and dissemination of scientific research findings to improve the prevention and treatment of substance use disorders and enhance public awareness of addiction as a brain disorder.

  - The NLM is the world's largest biomedical library; it has a vast print collection and electronic information resources, including comprehensive on-line resources for prescription drug information. NLM also supports and conducts research, development, and training in biomedical informatics and health information technology.

- AHRQ – The Agency for Healthcare Research and Quality's mission is to produce evidence to make healthcare safer, of higher quality, more accessible, equitable, and affordable, and to work within the HHS and with other partners to make sure that the evidence is understood and used. AHRQ collects medical expenditure information, including drug-use data related to prescribed medicine purchases.

B.2 Department of Justice

The DOJ has two organizations that have significant roles in prescription drug oversight:

- DEA – The Drug Enforcement Agency enforces the controlled substances laws and regulations of the United States and brings to the criminal and civil justice system of the United States, or any other competent jurisdiction, those organizations and principal members of organizations, involved in the growing, manufacture, or distribution of controlled substances appearing in or destined for illicit traffic in the United States; and recommends and supports non-enforcement programs aimed at reducing the availability of illicit controlled substances on the domestic and international markets.
- BJA – the Bureau of Justice Assistance Office provides grants, training and technical assistance, and policy development services to state, local, and tribal governments to reduce violent and drug-related crime, support law enforcement, and combat victimization. This includes activities targeted at opioid abuse and state-run prescription drug monitoring programs (see Section 2.4.5).

B.3 United States Pharmacopeia

The USP is a private, nonprofit, standards-setting organization whose mission is to advance public health, in part, by ensuring the quality and consistency of medications and promoting their safe and proper use. USP sets standards for the identity, strength, quality, and purity of medicines manufactured, distributed, and consumed in the United States and more than 140 other countries. Under the statutory authority of the 1906 Pure Food and Drug Act, USP maintains this information in the dual-compendia by the United States Pharmacopeia and National Formulary (USP-NF) (21 U.S.C. 321(j)).[49,50] The dual compendia have monographs for drug substances, dosage forms, and compounded preparations, while monographs for

[49] Section 1860D-4(b)(3)(C)(ii) of the Medicare Prescription Drug Improvement and Modernization Act of 2003 mandates that the FDA request that the United States Pharmacopeial Convention (USP) develop model guidelines, "… in consultation with pharmaceutical benefit managers and other interested parties, a list of categories and classes that may be used by prescription drug plans … and to revise such classification from time to time to reflect changes in therapeutic uses of covered [Medicare] Part D drugs and the additions of new covered Part D drugs."

[50] In the United States, the Federal Food, Drug, and Cosmetic Act defines "official compendium" to mean "… the official United States Pharmacopeia … official National Formulary, or any supplement to any of them."

excipients (critical non-medicinal ingredients) are in the National Formulary.[51,52] USP's standards are adopted and used by organizations outside the United States, including more than 140 countries. Under FDA regulation, drug products in the United States must conform to the quality standards in the USP-NF to avoid possible charges of adulteration and misbranding (21 CFR 299.5).

[51] A monograph includes the name of the ingredient or preparation; the definition; packaging, storage, and labeling requirements; and the specification. The specification consists of a series of tests, procedures for the tests, and acceptance criteria.

[52] The USP-NF is primarily of use to drug establishments and is available via subscription through USP at https://www.uspnf.com/.

Appendix C – Additional Drug Information Sources

The list of additional drug information sources includes the U.S. Food and Drug Administration (FDA) sources that were briefly discussed in Section 2.3.1:

- **National Drug Code (NDC) Directory**: https://www.fda.gov/drugs/informationondrugs/ucm142438.htm

  The NDC Directory lists all drug products along with their individual, assigned NDC, a unique 10-digit, 3-segment number. The NDC is a universal product identifier for human drugs in the United States. The NDC Directory tabulates information submitted electronically by labelers to the FDA.[53] The NDC Directory lists proprietary and generic drug names, delivery form and route, dose, marketing start and end dates, labeler, and other information, but the information is not verified by the FDA.

- **Drugs@FDA database**: https://www.accessdata.fda.gov/scripts/cder/daf/

  Drugs@FDA contains information about the FDA-approved prescription and over-the-counter drugs for human use. It includes most of the drugs approved after the passage of the Federal Food, Drug, and Cosmetic Act (FD&C Act) in 1938. The majority of patient information, labeling, approval letters, reviews, and other information are available for drugs approved since 1998.

- **FDA Orange Book**: Approved Drug Products with Therapeutic Equivalence Evaluations: https://www.accessdata.fda.gov/Scripts/cder/ob/index.cfm

  The Orange Book lists all prescription drug products that are FDA-approved, along with therapeutic equivalence determinations (i.e., generics) for multisource prescription products. The Orange Book also has information about over-the-counter medications, biologics, and approved drug products that have never been marketed.

- **DEA Orange Book**: https://www.deadiversion.usdoj.gov/schedules/index.html

  The Drug Enforcement Agency (DEA) Orange Book provides an on-line portal to information, including lists, about controlled substances. DEA cautions, “This document [Orange Book] is a general reference and not a comprehensive list. This list describes the basic or parent chemical and does not describe the salts, isomers and salts of isomers, esters, ethers and derivatives which may also be controlled substances.”

- **DailyMed**: https://dailymed.nlm.nih.gov/dailymed/index.cfm

  DailyMed is published by the National Library of Medicine and is the official provider of FDA label information (package inserts). The information is the most recent submitted to the FDA and currently in use. The specific package insert and label information is provided by brand or generic name, drug form (e.g., tablet, injection, etc.), NDC code, and packager.

[53] A labeler may be either a manufacturer, including a repackager or relabeler, or, for drugs subject to private labeling arrangements, the entity under whose own label or trade name the product will be distributed.

- **RxNORM**: https://www.nlm.nih.gov/research/umls/rxnorm/index.html

  RxNorm provides normalized names for clinical drugs and links its names to many of the drug vocabularies commonly used in pharmacy management and drug interaction software. RxNorm includes the United States Pharmacopeia (USP) Compendial Nomenclature from the United States Pharmacopeial Convention. USP is a cumulative data set of all active pharmaceutical ingredients. RxNorm maps to the USP Medicare Model Guidelines and USP Drug Classification (described in Section 2.3.2).

- **NIH Drug Information Portal Resources**: https://druginfo.nlm.nih.gov/drugportal/jsp/drugportal/consumerDrugs.jsp

  This National Institutes of Health consumer resource provides links to a wide range of information resources.

Appendix D – NRC Job Categories

The U.S. Nuclear Regulatory Commission's (NRC's) Fitness for Duty (FFD) program categorizes labor at Title 10 of the *Code of Federal Regulations* Part 26, Section 4 (10 CFR 26.4) by duties performed, including those performed by operators, emergency response staff, maintenance workers, and security staff. The defined job categories are as follows:

- Operators: Operating or onsite directing of the operation of systems and components that a risk-informed evaluation process has shown to be significant to public health and safety;
- Emergency response:
  - Performing health physics or chemistry duties required as a member of the onsite emergency response organization minimum shift complement;
  - Performing the duties of a fire brigade member who is responsible for understanding the effects of fire and fire suppressants on safe shutdown capability;
- Maintenance: Performing maintenance or onsite directing of the maintenance of structures, systems and components (SSCs) that a risk-informed evaluation process has shown to be significant to public health and safety; and
- Security: Performing security duties as an armed security force officer, alarm station operator, response team leader, or watchman, hereinafter referred to as security personnel.

Beyond these defined job categories, the NRC FFD program also applies to other individuals, including those who have unescorted access to protected areas, must physically report to the licensee's Technical Support Center or Emergency Operations Facility, have responsibilities for Category IA material, or create or have access to procedures or records for safeguarding strategic special nuclear material (SSNM). The NRC FFD program also applies during the construction of safety- or security-related SSCs for workers, supervisors, and managers.

Tables D-1 through D-5 provide more detail about the work duties defining a covered individual.

Table D-1. FFD applicability to individuals who have duties or perform activities at SSNM licensee facilities.

Citation	Duty or Activity for Individuals for SSNM Licensees in § 26.3(b)	Exception
§ 26.4(d)(1)	All persons who are granted unescorted access to Category IA material	Subparts I & K
§ 26.4(d)(2)	All persons who create or have access to procedures or records for safeguarding SSNM	Subparts I & K
§ 26.4(d)(3)	All persons who measure Category IA material	Subparts I & K
§ 26.4(d)(4)	All persons who transport or escort Category IA material	Subparts I & K
§ 26.4(d)(5)	All persons who guard Category IA material	Subparts I & K
§ 26.4(h)	Individuals who have applied for authorization for the above	See rule.[(a)]

(a) Pre-authorization requirements relate primarily to pre-access drug testing and protection of personal information.

Table D-2. FFD applicability to individuals who have unescorted access to nuclear power plant protected areas.

Citation	Duty for Individuals with Unescorted Access to Nuclear Power Plant Protected Areas by the Licensees in § 26.3(a) and, as applicable, (c)	Exception
§ 26.4(a)(1)	Operating or onsite directing of the **operation of systems and components** that a risk-informed evaluation process has shown to be significant to public health and safety	Subpart K
§ 26.4(a)(2)	Performing **health physics or chemistry duties** required as a member of the onsite emergency response organization minimum shift complement	Subpart K
§ 26.4(a)(3)	Performing the duties of a **fire brigade member** who is responsible for understanding the effects of fire and fire suppressants on safe shutdown capability	Subpart K
§ 26.4(a)(4)	Performing **maintenance or onsite directing of the maintenance** of SSCs that a risk-informed evaluation process has shown to be significant to public health and safety	Subpart K
§ 26.4(a)(5)	Performing security duties as an armed security force officer, alarm station operator, response team leader, or watchman, hereinafter referred to as **security personnel**	Subpart K
§ 26.4(b)	Do not perform the duties described in paragraph § 26.4(a)	§§ 26.205 through 26.209 and Subpart K
§ 26.4(c)	Physically report to the licensee's Technical Support Center or Emergency Operations Facility by licensee emergency plans and procedures	§§ 26.205 through 26.209 and Subpart K
§ 26.4(h)	Individuals who have applied for authorization for the above duties.	See rule.[(a)]

(a) Pre-authorization requirements relate primarily to pre-access drug testing and protection of personal information.

Table D.1. Applicability to individuals at nuclear power plant construction sites.

Citation	Duty for Individuals at Nuclear Power Plant Construction Sites in § 26.3(c)	Exception
§ 26.4(e)(1)	Serves as security personnel required by the NRC, until the licensees or other entities receive special nuclear material in the form of fuel assemblies, at which time individuals who serve as security personnel required by the NRC must meet the requirements applicable to security personnel in paragraph (a)(5) of this section	Subparts I & K
§ 26.4(e)(2)	Performs quality assurance, quality control, or quality verification activities related to safety- or security-related construction activities	Subparts I & K
§ 26.4(e)(3)	Based on a designation under § 26.406 by a licensee or other entity, monitors the fitness of the individuals specified in paragraph (f) of this section	Subparts I & K
§ 26.4(e)(4)	Witnesses or determines inspections, tests, and analyses certification required under Part 52 of this chapter	Subparts I & K
§ 26.4(e)(5)	Supervises or manages the construction of safety- or security-related SSCs	Subparts I & K
§ 26.4(e)(6)	Directs, as defined in § 26.5, or implements the access authorization program, including access to information used in authorization decisions, making authorization decisions, see rule for more details	Subparts I & K
§ 26.4(f)	Constructing or directing the construction of safety- or security-related SSCs	Subparts I & K or Meet all of Subpart K

Table D.2. FFD program applicability for program personnel.

Citation	Access or activities for FFD program personnel at NPPs and other entities (§ 26.3(a) through (c), and, as applicable, (d))	Exception
§ 26.4(g)(1)	All persons who can link test results with the individual who was tested before an FFD policy violation determination is made, including, but not limited to the MRO	Subparts I & K
§ 26.4(g)(2)	All persons who make determinations of fitness	Subparts I & K
§ 26.4(g)(3)	All persons who make authorization decisions	Subparts I & K
§ 26.4(g)(4)	All persons involved in selecting or notifying individuals for testing	Subparts I & K
§ 26.4(g)(5)	All persons involved in the collection or onsite testing of specimens	Subparts I & K

Table D.3. Individuals exempt from the NRC FFD program.

Citation	Exempt individuals	Exception
§ 26.4(i)	Individuals who are not employed by a licensee or other entity, and whose normal workplace is not at the licensee's or other entity's facility, but who may be called on to provide an FFD program service. These include: • medical professionals • NRC employees and other emergency or law enforcement personnel • other individuals regulated under other FFD programs.	All – explicitly exempt from the NRC FFD program
§ 26.4(j)	Individuals who are subject to this part and who are also subject to a program regulated by another Federal agency or State need be covered by only those elements of an FFD program that are not included in the Federal agency or State program, as long as the other agency's FFD program includes mandatory program elements (e.g., drug testing, training, licensee/other entity violation notification).	See rule for detail

Appendix E – Side Effects of the Top 20 Prescription Drugs

Table E-1 lists drug side effects for the top 20 prescription drugs from the 2019 ClinCalc DrugStats Database that estimates prescription drug-use data for patients in the United States (https://clincalc.com/DrugStats/Top300Drugs.aspx). The ClinCalc DrugStats Database is a sanitized and standardized version of the Medical Expenditure Panel Survey conducted by the U.S. Department of Health and Human Services' Agency for Healthcare Research and Quality. Each drug may have more than one manufacturer and multiple forms and dosages. Side effect information in this table was collected from the National Library of Medicine's MedlinePlus list of side effects (https://medlineplus.gov/). The side effect descriptions are not standardized and are listed here essentially as reported by MedlinePlus. There may be other side effects, including those that are simply less common or serious side effects that are indications of overdose or need for medical intervention and thus should not be encountered in the working population. Note that a side effect for one drug may be indication of a serious side effect for another (e.g., rash for lisinopril vs. gabapentin). Further, when users stop taking certain drugs, they may have withdrawal symptoms that are not listed here (e.g., suddenly stopping sertraline can cause a myriad of serious withdrawal symptoms including nausea, sweating, depression, mood changes, frenzied or abnormally excited mood, irritability, anxiety, confusion, dizziness, headache, tiredness, seizures, ringing in the ears, numbness or tingling in the arms, legs, hands, or feet, difficulty falling asleep or staying asleep).

Table E-1. Side effects of the top 20 prescription drugs.

	Top 20 Prescription Drugs (Drug Enforcement Agency schedule if applicable)																			
Side Effect	**Levothyroxine**	**Lisinopril**	**Atorvastatin**	**Metformin**	**Amlodipine**	**Metoprolol**	**Omeprazole**	**Simvastatin**	**Losartan**	**Albuterol**	**Gabapentin**	**Hydrochlorothiazide**	**Acetominophen; Hydrocodone Bitartrate**	**Sertraline Hydrochloride**	**Furosemide**	**Fluticasone[a]**	**Acetaminophen**	**Amoxicillin**	**Alprazolam (IV)**	**Atenolol**
Changes in Appetite	■																		■	
Increased appetite											■									
Increased or decreased appetite										■										
Loss of appetite												■		■						
Bloating				■																
Gas			■	■			■													
Gas or bloating						■														
Constipation				■		■	■	■			■			■	■				■	
Diarrhea	■	■	■	■					■		■	■		■	■			■		■
Heartburn			■			■			■		■			■						
Indigestion				■																
Nausea		■				■		■		■	■			■				■	■	■

Side Effect	Top 20 Prescription Drugs (Drug Enforcement Agency schedule if applicable)																			
	Levothyroxine	Lisinopril	Atorvastatin	Metformin	Amlodipine	Metoprolol	Omeprazole	Simvastatin	Losartan	Albuterol	Gabapentin	Hydrochlorothiazide	Acetominophen; Hydrocodone Bitartrate	Sertraline Hydrochloride	Furosemide	Fluticasone[a]	Acetaminophen	Amoxicillin	Alprazolam (IV)	Atenolol
Stomach Pain				■	■	■		■												
Upset Stomach					■															
Vomiting	■					■	■				■			■				■		
Changes in taste																		■		
Dry mouth											■			■					■	
Dry throat													■							
Increased salivation																			■	
Unpleasant metallic taste in mouth				■																
Back or joint pain											■									
Joint Pain	■		■																■	
Leg, Knee, or Back pain									■											
Excessive Tiredness		■												■						
Leg Cramps	■																			
Muscle cramps or weakness									■											
Muscle Pain				■																
Tiredness						■													■	■
Tiredness or weakness											■									
Weakness		■																		
Confusion			■					■												
Difficulty concentrating																			■	
Fuzzy thinking													■							
Strange or unusual thoughts											■									
Forgetfulness or memory loss			■					■												
Memory problems											■									
Abnormally happy or													■							

Side Effect	Top 20 Prescription Drugs (Drug Enforcement Agency schedule if applicable)																			
	Levothyroxine	Lisinopril	Atorvastatin	Metformin	Amlodipine	Metoprolol	Omeprazole	Simvastatin	Losartan	Albuterol	Gabapentin	Hydrochlorothiazide	Acetominophen; Hydrocodone Bitartrate	Sertraline Hydrochloride	Furosemide	Fluticasone[a]	Acetaminophen	Amoxicillin	Alprazolam (IV)	Atenolol
abnormally sad mood													■							
Anxiety											■		■							
Depression						■														■
Irritability																			■	
Nervousness										■				■						
Sudden changes in mood										■										
Decreased sensitivity to touch									■											
Ringing in the ears														■						
Sensitivity to heat	■																			
Difficulty falling asleep or staying asleep										■				■						
Drowsiness					■						■		■						■	■
Excessive motion or activity										■										
Shakiness										■										
Uncontrollable shaking of a part of the body										■	■			■						
Unwanted eye movements											■									
Dizziness		■								■	■			■					■	■
Dizziness or Lightheadedness					■	■														
Lightheadedness																			■	■
Unsteadiness											■									
Blurred vision															■					
Double or blurred vision											■									
Headache	■			■	■		■	■		■	■	■		■	■	■		■	■	
Talkativeness																			■	
Changes in menstrual cycle	■																			

Side Effect	Top 20 Prescription Drugs (Drug Enforcement Agency schedule if applicable)																		
	Levothyroxine	Lisinopril	Atorvastatin	Metformin	Amlodipine	Metoprolol	Omeprazole	Simvastatin	Losartan	Albuterol	Gabapentin	Hydrochlorothiazide	Acetominophen; Hydrocodone Bitartrate	Sertraline Hydrochloride	Furosemide	Fluticasone[a]	Acetaminophen	Amoxicillin	Alprazolam (IV)	Atenolol
Changes in sex drive or ability														■					■	
Decrease in sexual ability		■																		
Excessive sweating														■						
Flushing					■															
Flushing of the skin				■																
Hair Loss	■											■								
Itching													■							
Nail changes				■																
Pale skin										■										
Rash		■											■							
Rash or Itching						■														
Red, itchy eyes (sometimes with swelling or discharge)											■									
Weight changes														■					■	
Weight gain											■									
Weight gain or loss	■																			
Cold hands and feet						■														
Difficulty urinating													■						■	
Ear infection																■				
Ear pain											■									
Fever	■										■					■				
Frequent urination												■			■					
Narrowing of the pupils													■							
Swelling of the hands, feet, ankles, or lower legs					■						■									
Cough		■																		
Hoarseness																■				

	Top 20 Prescription Drugs (Drug Enforcement Agency schedule if applicable)																			
Side Effect	**Levothyroxine**	**Lisinopril**	**Atorvastatin**	**Metformin**	**Amlodipine**	**Metoprolol**	**Omeprazole**	**Simvastatin**	**Losartan**	**Albuterol**	**Gabapentin**	**Hydrochlorothiazide**	**Acetominophen; Hydrocodone Bitartrate**	**Sertraline Hydrochloride**	**Furosemide**	**Fluticasone[a]**	**Acetaminophen**	**Amoxicillin**	**Alprazolam (IV)**	**Atenolol**
Nose bleed										■										
Runny nose		■				■														
Runny nose, sneezing, cough, sore throat, or flu-like symptoms											■									
Sneezing		■																		
Sore or irritated throat																■				
Stuffy or runny nose																■				

(a) Side effects for fluticasone oral inhalation.

Appendix F – HHS-Certified Laboratories for 2018

Table F-1 presents the HHS-certified laboratories listed in 2018 *Federal Register* notices.

Table F-1. HHS-certified laboratories listed in 2018 *Federal Register* notices.

Laboratory	Location	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
ACM Medical Laboratory, Inc.	Rochester, NY	X	X	X	X	X	X	X	X	X	X	X	X
Alere Toxicology Services	Gretna, LA	X	X	X	X	X	X	X	X	X	X	X	X
Alere Toxicology Services	Richmond, VA	X	X	X	X	X	X	X	X	X	X	X	X
Baptist Medical Center-Toxicology Laboratory	Little Rock, AR	X	X	X	X	X	X	X	X	X	X	X	X
Clinical Reference Laboratory, Inc.	Lenexa, KS	X	X	X	X	X	X	X	X	X	X	X	X
Cordant Health Solutions(a)	Tacoma, WA										X	X	X
DrugScan, Inc.	Horsham, PA	X	X	X	X	X	X	X	X	X	X	X	X
Dynacare	London, ONT, Canada	X	X	X	X	X	X	X	X	X	X	X	X
ElSohly Laboratories	Oxford, MS	X	X	X	X	X	X	X	X	X	X	X	X
Laboratory Corporation of America Holdings	Houston, TX	X	X	X	X	X	X	X	X	X	X	X	X
Laboratory Corporation of America Holdings	Raritan, NJ	X	X	X	X	X	X	X	X	X	X	X	X
Laboratory Corporation of America Holdings	Research Triangle Park, NC	X	X	X	X	X	X	X	X	X	X	X	X
Laboratory Corporation of America Holdings	Southaven, MS	X	X	X	X	X	X	X	X	X	X	X	X
LabOne, Inc. d/b/a Quest Diagnostics	Lenexa, KS	X	X	X	X	X	X	X	X	X	X	X	X
MedTox Laboratories, Inc.	St. Paul, MN	X	X	X	X	X	X	X	X	X	X	X	X
Legacy Laboratory Services—MetroLab	Portland, OR	X	X	X	X	X	X	X	X	X	X	X	X

Laboratory	Location	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Minneapolis Veterans Affairs Medical Center, Forensic Toxicology Laboratory	Minneapolis, MN	X	X	X	X	X	X	X	X	X	X	X	X
National Toxicology Laboratories, Inc.	Bakersfield, CA	X	X	X	X	X	X	X	X	X	X	X	X
One Source Toxicology Laboratory, Inc	Pasadena, TX	X	X	X	X	X	X	X	X	X	X	X	X
Pacific Toxicology Laboratories	Chatsworth, CA	X	X	X	X	X	X	X	X	X	X	X	X
Pathology Associates Medical Laboratories	Spokane, WA	X	X	X	X	X	X	X	X	X	X	X	X
Phamatech, Inc	San Diego, CA	X	X	X	X	X	X	X	X	X	X	X	X
Quest Diagnostics Incorporated	Tucker, GA	X	X	X	X	X	X	X	X	X	X	X	X
Quest Diagnostics Incorporated	Norristown, PA	X	X	X	X	X	X	X	X	X	X	X	X
Quest Diagnostics Incorporated(b)	West Hills, CA	X	X	X									
Redwood Toxicology Laboratory	Santa Rosa, CA	X	X	X	X	X	X	X	X	X	X	X	X
STERLING Reference Laboratories	Tacoma, WA	X	X	X	X	X	X	X	X	X			
U.S. Army Forensic Toxicology Drug-Testing Laboratory	Fort George G. Meade, MD	X	X	X	X	X	X	X	X	X	X	X	X

(a) Formerly: STERLING Reference Laboratories, changed October 2018.

(b) Voluntarily withdrew from the National Laboratory Certification Program effective March 16, 2018.

Data Source: Federal Register Announcements from 2018.

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