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Panel on Effective Drug Control Strategies in Northern Cyprus:
Challenges and Opportunities in 2024

CONTROLLED PSYCHOACTIVE SUBSTANCES AND
WORKPLACE DRUG TESTING

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Abstract

The use of psychoactive substances has been on the rise around the world. Psychoactive substances, such as amphetamine, codeine, cocaine, marijuana, methamphetamine, etc. have potent pharmacological activities that cause cognitive and behavioral disorders. New psychoactive substances (NPSs) have also emerged that produce similar effects to those induced by illegal drugs, such as cocaine, cannabis, and amphetamines, but are not strictly regulated by international conventions. The rapid emergence since the mid-2000s of a large and diverse range of substances termed new psychoactive substances originally designed as legal alternatives to more established illicit drugs has challenged traditional approaches to drug monitoring, surveillance, control, and public health responses. Drug testing is an application used for detected substance use or abuse evaluation processes. As substance use affects human health and safety for not only the person who uses the substance, but also the people around him who do not use it in workplace areas. Therefore, drug testing is used in clinical and forensic purposes in employment, educational, and legal settings. These tests ensure that employers and employees comply with the legal regulations while also helping to lessen business accidents and workplace crime, improve business quality and productivity, and promote drug use avoidance. There have been many scientific, technical, and legal challenges to the validity of urine drug testing. This paper presents definitional information on the terms of psychoactive substances use, legislation of drugs and explores challenges and opportunities for drug monitoring with a view to public health and public safety.

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1. Introduction

Psychoactive substances are compounds that can either stimulate or inhibit the central nervous system or cause psychoactive effects to the extent that their use has been prohibited globally. According to the World Health Organization, 'substance abuse' refers to the hazardous use of psychoactive substances that includes alcohol, tobacco, psychoactive clinical drugs, and illicit substances (Abbott et al., 2020). The use of psychoactive substances has been on the rise around the world. According to United Nations Office on Drugs and Crime (UNODC)'s 2023 Drug Report, in 2021, 1 in every 17 people aged 15–64 in the world had used a drug. The estimated number of users grew from 240 million in 2011 to 296 million in 2021 and this shows a 23% increase, partly due to population growth (UNODC, 2023). Psychoactive substances, such as amphetamine, codeine, cocaine, marijuana, methamphetamine, etc. have potent pharmacological activities that cause cognitive and behavioural disorders (Baker & Kasprzyk-Hordern, 2011).

Substance use, which is an interdisciplinary problem, is combated with inter-institutional coordination. Countries and international commissions have created legal regulations and policies to combat the substance. The purpose of these legislations is to prevent the abuse of psychoactive substances and ensure their usability for medical and scientific purposes. The Convention of 1961, aimed at combating the use of illicit drugs by coordinated international action. With the emergence of new psychoactive substances such as amphetamine-type stimulants (e.g. "ecstasy"), Member States of Commissions found it necessary to conclude a new agreement, and thus the 1971 Convention emerged. The Commission on Narcotic Drugs-CND assists in the implementation and monitoring of international drug control agreements by the United Nations Economic and Social Council. In 1991, the Council plenary expanded the Commission's mandate to enable it to function as the governing body of the United Nations Office on Drugs and Crime (United Nations, 1961). In Türkiye, the import, export, and sale of psychoactive substances, are prohibited in accordance with Article 3 of the "Law on the Control of Narcotic Drugs" of the Turkish Penal Code 2313 and 5237. Many countries restrict substances by listing them for their risk of abuse or medical use; thus meeting their international drug control agreement obligations. Turkish Drug and Drug Addiction Monitoring Centre (TUBİM) Directorate, which works in coordination with UNODC and EMCDDA (European Monitoring Centre for Drugs and Drug Addiction), is responsible for monitoring all aspects of substance use and coordinating the institutions operating in this field.

New psychoactive substances (NPSs) have also emerged that produce similar effects to those induced by illegal drugs, such as cocaine, cannabis, and amphetamines, but are not strictly regulated by international conventions (Bijlsma et al., 2019). The increase in the use of new psychoactive substances in recent years has led to an increase in many crimes and legal situations related to deficiencies in regulations. The rapid emergence since the mid-2000s of a large and diverse range of substances originally designed as legal alternatives to more established illicit drugs termed new psychoactive substances has challenged traditional approaches to drug monitoring, surveillance, control, and public health responses (Peacock et al., 2019).

EMCDDA has established early warning groups called EWS (Early Warning System) to facilitate the fight against new psychoactive substances. These groups share reports to EMCDDA with all member countries expediting the enforcement of early measures against the substance. If these reports that a newly released substance exceeds a certain size, EMCDDA convenes the extended scientific committee together

with Europol and prepares a joint report on the substance. Joint reports include the chemical and physical description of the substance, its street name, the amount and form of seizures, the number of users, how they change hands, the production method, drug traffic, health and social risks in users, the presence of poisoning and death due to the substance, and chemical precursors. If the report concludes that the substance is dangerous, member states are requested to legalise enforcement against the substance within 180 days (EMCDDA, 2002; TUBİM, 2012).

The growing non-medical use of prescription drugs is also a global health concern as NPSs. The market for drugs is diversifying, and new psychoactive substances continue to appear with new drug combinations, mostly mixtures of controlled drugs. The real scale of the problem is unknown, due partly to lack of data on the non-medical use of prescription drugs, and partly to the existence of many gaps in the monitoring of their legal use for medical purposes as prescribed by healthcare professionals (Aydoğdu et al., 2021). Advances in the pharmaceutical industry have led to the production of powerful psychoactive medications, which when prescribed appropriately and taken in the manner intended, improve the quality of life of those with specific medical conditions, such as acute pain, palliative care, epilepsy, dependence on opioids and acute anxiety. It is imperative that this system operates in a balanced manner in terms of health and human rights. The rapid expansion of psychoactive substances, which are also used medically, is a situation that requires particular attention in the fight against substance use.

Different drugs pose different burdens on health and health-care systems. Although such compounds are often developed by pharmaceutical companies, some are used only for recreational purposes. These compounds reach the black drug market and are sold as drugs (as new psychoactive substances, NPSs) (Zawilska & Wojcieszak, 2019). Most drug use disorders are related to opioids which remain the most lethal drug. There are clear regional differences in the primary drug reported by people entering drug treatment: in most of Europe and most of the sub regions of Asia, opioids are the most frequent primary drug of people in drug treatment (United Nations Office on Drugs and Crime [UNODC], n.d.). Besides opioids, drugs containing gabapentinoids (gabapentin and pregabalin) are widely prescribed for medical purposes in the fields of physical therapy and rehabilitation, orthopedics, algology, neurology, and psychiatry (Ovat et al., 2024). The United States Drug Enforcement Administration (DEA) classifies pregabalin as a Schedule V controlled substance, indicating the lowest abuse liability among scheduled drugs; moreover, gabapentin is not a DEA-controlled substance (Cairns et al., 2018). Pre-marketing studies have indicated that pregabalin has a low abuse potential. Pregabalin was among the 30 most prescribed drugs in the USA in 2011 (World Health Organization [WHO], 2018). Despite this, there have been numerous reports of misuse and abuse (Lottner-Nau et al., 2013; Servais et al., 2023; Yargic & Ozdemiroglu, 2011). People have misplaced perceptions that prescribed drugs are safer than illegal substances. This situation contributes to the increase in the consumption of controlled drugs.

This paper presents the definitional information of the scope of psychoactive substances uses, legislations of drugs and explores challenges and opportunities for drug monitoring in terms of public health and public safety. In the following sections, the purposes, applications, and difficulties experienced in drugs testing and workplace drug testing approach are presented.

2. Drug Testing

Drug testing is used for clinical and forensic purposes in different areas. Drug testing is requested: (i) to identify drugs in emergency department patients and allow initiation of appropriate intervention; (ii) as a tool to monitor drug use and adherence in treatment and rehabilitation programs (e.g. opiate dependency and pain management programs); (iii) to monitor medicinal agents prescribed for therapeutic reasons (therapeutic drug monitoring (TDM)) and; (iv) to identify drug use in the workplace (i.e. workplace drug testing). The main disciplines of forensic toxicology are post-mortem forensic toxicology, human performance toxicology, and forensic drug testing. Each of these programmes has a different objective as well as different technological and analytical requirements.

Drug testing can be completed on various biological specimens including urine, blood, hair, saliva, sweat, nails (toe and finger), and meconium (Aslan et al., 2023). Urine is the most obtained specimen for drug testing due to its non-invasive route and ease of sample collection. Both parent drug and metabolites may be detected in urine specimens and are usually in higher concentrations than in blood or serum samples.

The drug testing method chosen to detect a particular drug will depend on the reason for undertaking the test. Immunoassay drug tests are most used. They are designed to classify substances as either present or absent and are generally highly sensitive. A basic routine UDT panel should screen for the following drugs/drug classes: cocaine, amphetamines/methamphetamine (including Ecstasy), opiates, methadone, marijuana, and benzodiazepines. However, these panels are not always sufficient to detect all abused drugs/substances.

Specific drug identification using more sophisticated chromatographic analysis and methods is needed. Combined techniques such as gas or liquid chromatography make the accurate identification of a specific drug and its metabolites possible. Gas chromatography mass spectrometry (GC/MS) was used for determination of various abused drugs in biological matrixes. The GC/MS technique was the most used technique to separate and determine abused drugs and their metabolites due to its cost, high specificity, and sensitivity. However, GC/MS analysis required a derivatization process to increase the volatility of many polar analytes and the derivatization step is costly, time-consuming, and susceptible to errors. Liquid chromatography (LC) coupled with MS offers a powerful complement to immunochemical assays in clinical testing and is often the best method in forensic and clinical toxicology (Dresen et al., 2006; Kapur & Aleksa, 2020; Marquet et al., 2003; Marquet & Lachâtre, 1999).

New psychoactive substances introduced into the global drug market pose a significant risk to public health and safety. Testing for these NPS or designer drugs (e.g. synthetic cathinones and cannabinoids) is challenging as there is a continual change in synthetic compounds. Analyses of these drugs require a chromatographic (GC or LC-MS) approach (Kapur & Aleksa, 2020). For accurate and reliable analysis, reference methods should be developed, especially for the detection and identification of NPS and non-targeted toxicological screening.

2.1. Workplace Drug Testing (WDT)

Workplace drug testing has become widespread in many countries worldwide in recent years. It was first conducted in the United States in 1980 due to numerous railway accidents, which was then brought

into the agenda of both industry and the political parties in the fight against drugs (Verstraete & Pierce, 2001). In 1998, the European Workplace Drug Testing Society (EWDTS) was established and the WDT was implemented. With these developments, WDT has gained more importance in Europe, Australia, and other industrialized countries, consequently acquiring a broader application area in the last decade. These tests ensure that employers and employees comply with the legal regulations while also helping to lessen business accidents and workplace crime, improve business quality and productivity, and promote drug use avoidance.

Workplace drug testing is a drug test programme that can be applied to individuals:

- upon worker's recruitment randomly
- on a periodical basis
- on a suspicion basis
- after an accident at work
- at regular intervals.

The increase in the use of psychoactive legal/illegal substances in recent years has led to an increase in many crimes and many legal regulations related to these substances. Among these approaches, the drug testing system has been the area with the most development. Due to this, new applications for the substance abuse evaluation processes of rapidly developing drug tests have become mandatory. Substance use is considered a serious risk to safety and health not only for the person using the substance, but also for those around him who do not use it. In recent years, WDT has been widely carried out to minimize the harm that may occur in terms of productivity, workforce loss and employees' lives, and to ensure public safety.

Workplace drug testing is a substance testing program for individuals that can be implemented into workplaces through pre-employment screening (e.g., requiring urine samples from all job applicants) or post-employment surveillance (e.g., collecting random, comprehensive, or in case of suspicion urine samples from existing staff). There are many reasons why countries, institutions and companies implement WDT. These include: (i) To ensure that employers and employees comply with legal regulations; (ii) to reduce work-related accidents and workplace crimes; (iii) to increase work quality and productivity; and (iv) one of the most important reasons is to increase deterrence against substance use. In Northern Cyprus, the legal regulations and practices of workplace substance testing are defined with their legal frameworks within the scope of the Labor Law, Occupational Health and Safety Law, Workplace Medicine, and Transportation Regulations involving airlines, highways, and maritime transport (Akgür et al., 2012).

WDT involves three contact stages: (i) taking the sample; (ii) analysing the sample; and (iii) interpreting the analysis results. Forensic toxicological analyses have an important place in the process of substance use in biological materials in the workplace, which is limited by legal regulations. It is mandatory in international guidelines that the results of workplace substance tests, whose accuracy and reliability are crucial and which may also have legal sanctions, must be reported by experts in the field.

For WDT results to stand up in a court of law, the test must be done by at least two different methods that employ different physiochemical principles. The laboratory protocol also requires "chain-of-custody" for the sample that is being processed. Immunoassay is used to tentatively identify (presumptive positive) the drug class, while GC-MS and LC-MS/MS are used to confirm and identify the specific drug.

The primary screening test uses the immunoassay to detect the presence of psychoactive substances or their metabolites. The results of an immunoassay test are qualitative. In other words, the test result is

read as simply positive or negative (Akgür et al., 2022). Table 1 presents the cut-off values of the Substance Abuse and Mental Health Services Administration (SAMHSA) for drug testing and, the European Workplace Drug Testing Society (EWDTS) for workplace drug testing.

Table 1. Recommended Cut-off Concentrations (ng/ml) for screening analysis in SAMHSA and, EWDTS

Substance	SAMHSA and T.C Ministry of Health	EWDTS
Amphetamine	500	500
Benzodiazepine	300	200
Cannabinoid (THC-COOH)	50	50
Cocaine	150	150
Opiate	2000	300

(EWDTS, 2015; Swiss Guidelines Committee for Drug of Abuse Testing (SCDAT), n.d.)

For workplace drug testing, the EWDTS urine guidelines published two divided substances lists that have been arranged into primary and secondary groups, with primary substances representing the recommended core panel and secondary substances that are given as additional options based on the customer's needs (EWDTS, 2015) (see Table 2 below).

Table 2. Laboratory screening test cut-off concentration in urine (ng/mL)

Primary Substances	ng/ml
Amphetamines group	500
Benzodiazepines group	200
Cannabis metabolites	50
Cocaine metabolites	150
Methadone (or EDDP)	300 (100)
Opiates (total)	300
6-MAM	10
Secondary Substances	ng/ml
Barbiturates	200
Buprenorphine	5
Gabapentin	2000
Pregabalin	500
Ketamine	100
LSD or metabolites	1
Opioids (e.g., Oxycodone, Hydromorphone)	300
Phencyclidine	25
Propoxyphene or metabolites	300
Tamadol	200
Z-Drugs (e.g., Zopiclone, Zolpidem, Zaleplon)	200
Fentanyl	1

The crucial nature of the issue demands that it should be handled within the framework of global regulations and implemented within the scope of national policies in cooperation with the relevant national

and international institutions and organizations in the fight against these substances. In this context, the currency of these lists and the substances included in them is vital in order to institute accurate and effective analytical methods and substance use and performance evaluations used in many application areas - from substance tests performed in workplaces to analysis performed in wastewater. Gabapentoids potentiate the effects of opioids, increasing the risk of fatal overdose. People who use gabapentoids alongside opioids typically use them without a physician's prescription, likely self-medicating withdrawal symptoms or use the drug to induce euphoria and relaxation. The first reports of pregabalin abuse and dependence appeared in 2006. Finland reported an increase in deaths related to overdose and a number of deaths in which gabapentoids (pregabalin and gabapentin) were detected, mainly in the context of polydrug use with opioids.

The non-medical use of prescription drugs is a complex multi-faceted issue (Teker et al., 2023). At this point, it is vital to differentiate between medical and illegal drug use/misuse/abuse. Although PGB is on the 'secondary substances list' in the EWDTS Urine Manual, it cannot be detected because PGB is not yet included in the routine testing scale in most clinical laboratories. This situation may result in the abuse of PGB especially by people under probation.

2.2. Challenges to Drug Test Results

Many scientific, technical, and legal challenges have arisen in relation to the validity of urine drug testing. The process of drug testing associated with positive results are especially met with such challenges because they are often intertwined with constitutional and legal rights of individuals. There is often conflict between labour laws and the infringement of personal privacy rights (Phan et al., 2012). For this reason, it is crucial to produce accurate results, especially since tests such as workplace drug tests can have a first-degree impact on people's work, family, and social situations.

Due to the increasing trends of use of psychoactive substances, the measures taken, and policies implemented in many countries are changing. Adjusting cut-off values depend on the situation such as clinical needs, forensic requirements, as well as the current situation of world drug use trends. This also needs to be regulated by laboratories' administrative decisions, and legal procedures pertaining to forensic and clinical cases.

Forensic toxicology is a branch of forensic science that deals with the systematic collection and interpretation of evidence to solve crimes. The most relevant class of target analytes of forensic analysis are prescription drugs, drugs that are abused, new psychoactive substances, and alcohol biomarkers. Thus, the interpretation of drug testing is a challenging process and requires highly trained staff to both operate and interpret the results. As stated earlier, the non-medical use of prescription drugs is a complex multi-faceted issue which can be contentious in terms of the scientific, technical, and legal parameters.

However, with the enhanced awareness of forensic toxicology, laboratories can ensure justice in workplace drug testing, with a carefully thought-out testing strategy and accurate interpretation of the results.

3. Recommendations for the Northern Cyprus

This paper briefly summarizes that the worldwide scope of the drug use problem and provides effective applications for prevention and monitoring drug use, to ensure the safe and drug-free workplaces. It is obvious that the increasing use of psychoactive drugs and substances will significantly affect the social pattern and the development of society. In this context, a successful road map to reduce and prevent the harms that may arise from the use of psychoactive substances can be attained for Türkiye and Northern Cyprus, with the right cooperation from all the agencies concerned within the scope of the policies to be developed.

Declaration of Conflicts Interests

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