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Adulterants in illicit drugs: a review of empirical evidence

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Widespread public perception is that illicit drugs contain substances that are a serious risk to health, even though adulterants are often not considered in clinical or forensic toxicology. This review attempts to present an evidence-based overview of adulterants in illicit drugs, and their associated toxicity. Adulterants are deliberately added to increase bulk, enhance or mimic a pharmacological effect, or to facilitate drug delivery. Those present unintentionally are as a result of poor manufacturing techniques. From the reports gathered, adulterants are predominantly substances which are readily available, commonly being caffeine, procaine, paracetamol, and sugars. These are likely to have minimal impact on users' health at low dosages. Other adulterants, particularly in injectable drugs, have the potential to cause serious health issues, but the quantities reported, such as strychnine in heroin, are not life-threatening. The most commonly identified bacterial contaminants identified are Bacillus and Clostridium species. When death or serious illness due to adulteration occurs, circulation of information is particularly vital, such as in the USA regarding heroin and cocaine adulterated with fentanyl, and in Scotland recently regarding anthrax contaminated heroin.

The complex interactions of supply, demand, and control of illicit drugs have a tangible impact on their adulteration. Continuing vigilance and the circulation of information is, therefore, desirable as a public health issue. As part of that strategy, analyses performed for adulterants needs to be encouraged, which are considerably limited in number and scope at the moment. Copyright © 2010 John Wiley & Sons, Ltd.

Keywords: illicit drugs; adulteration; contamination; evidence

Introduction

It is estimated that globally, between 155 and 250 million people used drugs (at least once) during 2008 (between 3.5% and 5.7% of the global population aged 15–64)^[1] with little or no understanding of the other compounds they could also be consuming. Historically,^[2,3] and more recently,^[4–6] it has been a common perception that illicit drugs typically contain other substances, in addition to the purported active ingredient, which can have serious adverse health consequences or even cause premature death. These perceptions, however, do not necessarily reflect actual illicit drug adulteration. Typically, 'adulterant' refers to pharmacologically active ingredients; 'contaminant' refers to the by-products of the manufacturing process, and 'diluent' refers to inert substances. For the purpose of this paper, adulterants, contaminants, and diluents are all referred to as 'adulterants'.

Adulterants typically suggested by drug dealers, drug users, and the general public include mannitol, sugars, gravy powder, chalk, codeine, rat poison, ground glass, household cleaning products, and brick dust. [4,6-8] Research has shown that much less adulteration actually takes place than is anecdotally perceived by drug users and dealers, and stories of illicit drugs cut with household cleaning products, brick dust, and ground glass are inaccurate and potentially created to explain overdose and death amongst drug users. [4,5] A recent study investigated users' perceptions of the composition of cocaine compared with the actual composition of analysed samples (provided by interviewees), and found that users were largely unaware of the actual content, with only 5 of 99 users correctly identifying at least one adulterant present in their own cocaine. [9] It is important to

consider that a drug dealer is essentially a business person who relies on repeat custom and therefore poisoning customers and cutting off a reliable income supply does not make good business sense. [4,5,10-12]

The reasons for adulterants in illicit drugs are often varied. Additional substances may be added to bulk, dilute, complement, or enhance the effects of the drugs. Others are present unintentionally, being additional elements as the result of manufacturing, production, or storage techniques, for example alkaloids, micro-organisms or other biological agents. A review of forensic literature relating to drug 'impurities' identified 48 additives reported in analyses of cocaine (35 pharmacologically active additives, 9 inert additives, and 4 volatile compounds) and 60 in heroin (5 alkaloids, 33 pharmacologically active additives, 13 inert additives, and 9 volatile compounds). [13] Research has shown that benign adulteration practices (meaning adulteration with non-harmful substances such as sugars or caffeine) are similar in the UK, the USA, Canada, and Australia. [4,5,10]

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All elements of the production, distribution, and preparation for use of illicit drugs are confounded by their illegal status, incompatible with the quality assurance, sterile production, and accurate dosage administration associated with Good Manufacturing Practice.^[14] There are public health effects of the lack of quality control of illicit drug manufacturing and distribution. Drug sellers and users can only make inadequate assessments of the quality, purity, and chemical composition of any drugs they buy, sell, or use. [15] It is important also to consider that substances used to adulterate drugs may also have been made in clandestine laboratories and may themselves be adulterated; for example, illicitly manufactured fentanyl has been found in street heroin.^[16]

The purpose of this review is to present an evidence-based overview of illicit drug adulteration, based on a previous in-depth report.[17]

Methods

Peer-reviewed literature and case reports were retrieved through the systematic searching of electronic sources and relevant websites. Searches of the health and social sciences, and toxicology literature were undertaken in the following databases: MEDLINE; Sociological Abstracts; TOXLINE; and PsycINFO. Search strategies detailing key terms were developed as appropriate to each database platform: for example, 'cannabis/', 'narcotics/', 'adulterant' and 'contamination'. There were no restrictions on the year of publication or country of origin, but only English-language papers were selected. The websites of international and national organisations for the control and surveillance of drugs were also searched for unpublished or 'grey' literature: for example, United Nations Office on Drugs and Crime (UNODC), National Institute on Drug Abuse (NIDA), and European Monitoring Centre for Drugs and Drug Addiction (EMCDDA).

All papers were first and second reviewed by two researchers. Approximately 1800 peer-reviewed articles were included in the first review. This stage used a broad selection criteria where a document was included if there was mention of one of the selected illicit drugs and details of adulteration including reference to specific adulterants. A total of 1381 articles were excluded after the first review. The second review further investigated the detail of adulteration provided in each paper and also excluded papers that did not include new information but referred to other studies; a further 172 articles were excluded. The remaining 247 articles were examined in-depth and relevant studies were included.

Results

A summary of the published evidence of drug adulterants found in multiple samples of illicit drugs is presented in Table 1. This table provides the potential reasons for inclusion and health effects of the most common adulterants that have been purposefully added or result from manufacture, storage, or distribution. Table 2 summarises common bacterial infections caused by adulterated illicit drugs.

The available evidence indicated that illicit drugs are most commonly adulterated with caffeine, procaine, paracetamol, procaine, and sugars (sucrose, lactose, dextrose, mannitol); these substances have been detected in multiple illicit drugs. There are a variety of reasons why particular substances are used as illicit drug adulterants. Most commonly to add bulk, enhance or mimic the purported ingredient, facilitate the administration of the drug, or as the result of poor or unsterile manufacturing, storage, or distribution. Some adulterants may be included in different illicit drugs for different reasons.

To add bulk

Adulterants which add bulk or dilute are usually relatively cheap, easily available, and legal. The evidence presented indicates that caffeine, paracetamol, and sugars are common bulking agents. These substances have minimal health impacts at low dosages. Caffeine and paracetamol may serve a dual purpose when used as adulterants, both bulking and mimicking the effect of a drug, depending on which drug the substance is added to (caffeine has stimulant properties similar to cocaine and amphetamine, and paracetamol has analgesic properties similar to heroin).

To enhance or mimic

The adulterants may have been chosen to enhance or mimic the illicit drugs effects, either to give the impression of a better quality drug or mask a poor quality product. For example: procaine and lidocaine have similar anaesthetic properties to cocaine; phenacetin has similar physical properties to cocaine; paracetamol has a similar bitter taste to (white) heroin; methylsulfonylmethane (MSM) looks physically similar to methamphetamine; and caffeine has similar (but milder) stimulant properties to cocaine, amphetamine, and ecstasy.

To facilitate administration

Some adulterants facilitate the administration of the illicit drug, specifically to make smoking the drug more efficient. Caffeine and procaine have been found to vaporize heroin at a lower temperature and therefore facilitate smoking. [18]

The result of poor or unsterile manufacturing techniques

A number of the adulterants detailed in Table 1 may be unintentional additions or the result of poor manufacturing techniques. For example, lead in drugs such as heroin and cocaine may be a by-product of the use of lead pots in manufacture^[19,20] and aluminium in cannabis may have resulted from an impure water supply. Table 2 indicates that the most common bacterial infections caused by adulterated illicit drugs were bacillus and clostridium species infections.

Discussion

Whilst the relative dangers of and risks associated with use of illicit drugs are well known and generally acknowledged, the potential dangers associated with drug adulterants are not generally considered in the same manner. The evidence shows that illicit drugs are more commonly adulterated with benign substances (such as sugars), substances that will enhance or mimic the illicit drugs (such as phenacetin in cocaine), or substances that will facilitate the administration of illicit drugs (such as caffeine in heroin) (Table 1). These findings support previous research which found that routine adulteration of illicit drugs with 'dangerous' 1 substances are spurious. [4-6,8,12,21,22]

 $^{^{\}rm 1}$ Coomber acknowledges that illicit drugs are dangerous substances. However in this context he is referring to substances such as brick dust, talcum powder, rat poison, ground glass, and household cleaning products.

rug Adulterant(s)	Licit use	Potential reason for presence as adulterant	Public health risks	Health consequences	Source(s)
licit Sucrose, lactose, rugs dextrose and mannitol	, Sugars	To dilute/add bulk; legally and readily available.	Inactive adulterants	Minimal risk of adverse health effects; can cause nasal irritation.	43-55
Lead	Soft, malleable metal	Heroin: potentially a by-product of the use of lead pots in illicit drug manufacture.	In low dosages lead poisoning can have mild effects.	Abdominal pain and cramping, headaches, anaemia, dizziness, nausea/vomiting, muscle weakness, seizures, coma, renal injury and CNS damage.	19, 20, 29, 56–62
		Methamphetamine: sometimes used in methamphetamine manufacture; poor manufacturing can result in lead residue in drug product.	Injecting of illicit drugs adulterated with lead cause severe adverse health effects.		
Caffeine	Psychoactive stimulant drug	Caffeine is legal, cheap and more readily available than illicit drugs.	In small doses there are few serious health repercussions; moderate to large doses can cause considerable harms.	Mood disturbances, induce anxiety, addictive, sleep disturbance and increases risk of a range of health problems.	9, 21, 23, 25, 27, 28, 33, 35, 37, 43–48, 50–55 63–68
		Heroin: vaporizes heroin at lower temperature when smoked – slightly increases efficiency.			
		Cocaine, amphetamine, methamphetamine and ecstasy: stimulant properties of caffeine can create similar, although usually milder, effects to the primary drug.			
Procaine	Local anaesthetic	Heroin: facilitates smoking of heroin and may relieve the pain of intravenous injection due to anaesthetic properties. Cocaine: similar anaesthetic and subjective effects as cocaine.	Risk of toxicity at high doses.	CNS problems, nausea, vomiting, dizziness, tremors, convulsions and anxiety.	21, 25, 27, 33, 44–46, 48, 50, 51, 64–67, 69
Paracetamol	Over-the-counter pain relief medication		Low dosages should have minimal impact; risk of toxicity at high doses.	Liver damage, gastro-intestinal effects and adverse effects when mixed with alcohol.	9, 21, 35, 44, 46, 48, 50 – 54, 64, 65, 67 – 69
		Heroin: analgesic effects and bitter taste of paracetamol may disguise poor quality heroin; may be used because it has similar melting point to heroin.			
Strychnine	Pesticide	A fine motor stimulant. Low doses act as a muscle stimulant.	Whilst it has only been reported in non-life threatening quantities, small increases could potentially be fatal.	Muscle spasm and opisthotonos (holding of body in awkward rigid position).	23, 24
		Heroin: enhances retention of heroin when volatized. Has only been found at non-life threatening quantities. Cocaine: reason for			
		non-life threatening			

Table 1.	(Continued)					
Drug	Adulterant(s)	Licit use	Potential reason for presence as adulterant	Public health risks	Health consequences	Source(s)
Heroin	Phenobarbital	Barbiturate	Psychoactive drug which facilitates smoking of heroin.	Risk of adverse effects from large dose(s) which may be life-threatening in injecting users who are hypersensitive.	Adverse effects from a large dose(s) are serious and may be life-threatening; death.	44, 45, 48, 50, 64, 67
	Quinine	Antimalarial medication	Bitter taste similar to heroin and may be used as a diluents; mimics the respiratory 'rush' felt by injecting heroin users shortly after administration.	Adverse effects from a large dose(s) are serious and may be life-threatening; can also cause a host of other adverse health reactions.	Acute renal failure, cinchonism, gastric disturbances, thrombosis and hypotension (IV use), CNS overstimulation and death.	46, 65, 70
	Clenbuterol	Asthma decongestant and bronchodilator drug ^a	Reason for inclusion unknown but may have been unintentional contamination.	Can cause poisoning at moderate to high dosages; low doses typically cause adverse cardiovascular effects	Cardiovascular effects, neuromuscular syndrome, mydriasis (excessive pupil dilation) and agitation.	71-74
	Scopolamine	Anticholinergic alkaloid	Colourless, odourless and tasteless and therefore not easily detectable.	Low doses cause sleepiness and drowsiness; high doses can cause euphoria.	Anticholinergic toxicity ^b and CNS depressant.	75, 76
Cocaine	Lidocaine	Local anaesthetic	Similar, but stronger, anaesthetic effects as cocaine and gives the impression of higher quality cocaine.	and CNS reactions	CNS problems, nausea, vomiting, dizziness, tremors and convulsions.	9, 25, 27, 28, 43, 46–48
	Phenacetin	Analgesic substance	Pain relieving properties and similar physical properties to cocaine.	many countries due	Analgesic nephropathy, haemolytic anaemia, methaemoglobi- naemia, kidney cancer and bladder cancer	9, 25 – 28
	Levamisole	An anthelmintic medication (used for expelling parasitic worms)	Unknown, however, it is theorised that it gives a more intense high.	, ,	Fever and agranulocytosis	9, 25, 77, 78
Methamp	shetamine Methylsulfon- ylmethane (MSM)	Naturally occurring in some foods and also marketed as a dietary supplement	MSM is readily available and is physically similar to methamphetamine (odourless, white, crystalline powder); methamphetamine adulterated with MSM creates the impression of high purity methamphetamine.	5 ,	None identified.	53, 79
MDMA	Amphetamine, methampheta mine	Illicit stimulant drugs	Amphetamines have similar properties to the stimulant effects of 'ecstasy' although these adulterants are not entactogens; amphetamine substances are often sold as, or in combination with, MDMA.	Moderate doses can cause a range of adverse health effects; adverse effects from a large dose(s) are serious and may be life-threatening.	Mood disturbances, induce anxiety, addictive, sleep disturbance and increase risk of a range of health problems.	35, 37, 80, 81

Table 1.	(Continued)					
Drug	Adulterant(s)	Licit use	Potential reason for presence as adulterant	Public health risks	Health consequences	Source(s)
	Paramethoxy- methamphetamine (PMMA), parame- thoxyamphetamine (PMA)	Illegal psychoactive chemical	Purposefully added to ecstasy due to stimulant properties.	Relatively unknown, but high dosages have caused death.	Death.	82, 83
Cannabis	Aluminium	Soft, malleable metal	Unknown, but aluminium contamination may have resulted from impure water supply.	Contribute to smoking related diseases;	Smoking related adverse health effect effects	30
	Glass		Unknown, but potentially to improve apparent quality and increase weight.	Inhalation of hot glass fumes.	Sore mouth, mouth ulcers, chesty persistent coughs, and a tight chest	31

^a Clenbuterol is only licensed for use as a medication in some countries.

^b An anticholinergic toxidrome typically consists of blurred vision; agitation; fever; urinary retention; dry, hot, flushed skin; and dilated pupils.

Bacterial infection	Public health risks	Health consequences	Source
Bacillus anthracis (anthrax): bacterium which creates spores which can infect the body through three forms: skin, inhalation or gastrointestinal. Produces lethal poisons and can cause death.	Common public health risks associated with bacterial infection caused by adulterated illicit drugs are cited below.	The health consequences of bacterial infections are relatively common across different bacterial infections and therefore have been listed together below.	38, 39
Bacillus cereus: soil-dwelling bacteria.	 Cross contamination to other individuals is possible from open wounds. 	Most infections can be cured if identified early and include: abscess or inflammation at injecting sites, respiratory problems, nausea and vomiting, tetanus, septicaemia, paralysis ^a , botulism ^a , gas gangrene, and death.	84
Clostridium botulinum: anaerobic, spore-forming bacterium.	• Contamination of injecting equipment.		41, 85, 86
Clostridium novyi: anaerobic, spore-forming bacterium.	 Many bacterium survive the heating process common with preparation of heroin for injection. 		87, 88
Clostridium sordellii: rare anaerobic bacterium.	•		89
Necrotizing fasciitis: deep soft tissue infection.			89, 90

Table 1 shows that a potential reason for the common use of caffeine, procaine, paracetamol, and sugars as adulterants may be related to their characteristics; they are legal and most are readily available (with the exception of procaine which requires a prescription or a license). Clinically, use of procaine as a local anaesthetic drug has been effectively replaced by lidocaine and evidence indicates that more recently, lidocaine has been commonly used to adulterate cocaine (Table 1). Reports of the purposeful adulteration of illicit drugs with toxic substances were identified, including the adulteration of heroin with strychnine, [23,24] however, the quantities reported were not life-threatening or haphazard to suggest accidental presence. Strychnine is a toxic, colourless, crystalline alkaloid commonly used as rat poison; it was once a widely prescribed medicine and although it is no longer advised for human consumption,

small quantities may not be harmful. However, small increases in dose could be potentially fatal. Strychnine has particularly been reported as an adulterant of a specific 'brand' of heroin (China White of Heroin No. 3).^[22] As the substance has been shown to increase the retention of heroin when volatized,^[18] it is assumed that reports of its use as an adulterant was to facilitate drug administration rather than malicious intent. This is not an assurance, however, that the use of strychnine and other poisons in illicit drug manufacturing does not have the potential to cause serious health issues. There are particular concerns about the addition of phenacetin, an analgesic which has been linked to bladder and kidney cancer, to cocaine and crack cocaine.^[9,25–28] Phenacetin was the most commonly found adulterant (detected in 54% of samples) in a recent study of street cocaine in France.^[9]

Cannabis was found to be less likely to be adulterated than illicit drugs sold in powder or tablet form, but reports of cannabis adulterated with lead, aluminium, and glass in recent years highlight the potential health risks of adulterants to cannabis users. [29–31] Hough *et al.* [32] found that two-thirds of UK cannabis growers interviewed chose to cultivate their own plants because of the perceived risks associated with adulteration of cannabis resin.

The evidence indicated that LSD is not typically adulterated^[33] and there was little evidence identified for the adulteration of ketamine and GHB, which are typically diverted from legitimate sources.^[34] Ketamine was found to be more likely to be used as an adulterant in other illicit drugs, such as ecstasy and methamphetamine.^[35–37]

Table 2 shows that bacterial infections caused by adulterated drugs were most commonly *bacillus* and *clostridium* species, and were most common amongst injecting drug users. [38,39] Although the research literature presents a wealth of information about drug users who have contracted bacterial infections, only a small proportion have been confirmed to be due to drug adulteration as opposed to unsterile preparation.

The clandestine and underground nature of illicit drug production and the complex interactions of supply, demand, and control have a tangible impact on drug adulteration and contamination and therefore a resulting impact upon the public health of drug users. The manufacturing process itself may create by-products which adulterate the final product, and the method of manufacturing employed will affect the final composition. The quality of the drug produced is highly dependent upon the skills and abilities of the producer combined with a range of other issues, including the resources available, production environment, distribution infrastructure and varied market and enforcement factors. The variation in substances used to adulterate illicit drugs contributes to the unpredictability of the drug's effects, including the potential for unknown or unexpected synergistic reactions, and health-related consequences.

The disruption of production, transportation, and distribution of illicit drugs and precursors (including reductions in legitimate imports) may have unexpected effects, such as: a significant change in the composition of a given drug; illicit drugs of lesser quality becoming available; a significant rise in the cost of illicit drugs; [1] the manufacture of illicit drugs from non-controlled preprecursor chemicals;^[1] and the creation of a gap in the market for drug dealers willing to take more 'risks' (including the use of violence and aggressive selling).^[40] For example, successful seizure of precursors from illicit sources can lead to clandestine manufacture of precursors or the production of other substances sold as another purported illicit drug. The precursor of choice for manufacture of MDMA (3,4-MDP-2-P) has been subject to restrictions in recent years, with producers using safrole oil instead. However, the successful disruption of safrole diversion has impacted upon the composition of ecstasy in recent years, with manufacturers now using safrole-rich oils instead. [1] Typically ecstasy no longer solely contains MDMA as the active ingredient, with many 'ecstasy tablets' containing a combination of MDMA analogues or other agents, such as PMA and PMMA.

Limitations of drug adulteration data

Reports of drug adulteration were examined from worldwide sources and revealed a lack of standardised forensic analysis and reporting practices. Representative sampling of illicit drug samples is not routinely undertaken to quantify and qualify the extent of adulteration; most forensic analysis is undertaken for legal reasons to provide evidence for prosecution. With case reports, analysis of drug samples is not routinely undertaken or drug samples may not be available for analysis, therefore the conclusion that health effects are caused by illicit drug adulteration may be uncertain in some cases. The majority of analysis is undertaken retrospectively following either a drug seizure or an adverse health effect in an individual or group of drug users. Specifically, the lack of standardised analyses, reporting and, in some cases, lack of detailed reporting, created difficulties in comparing adulteration practices over time and by country.

The majority of analysis techniques identify which additional substances are present in samples of illicit drugs but do not report on the overall composition of the drug and the proportions of adulterants found. Also, it is not standard practice to report the percentage of samples which contain no adulteration. Both of these pieces of information would provide further useful information about adulteration practices but it is understood that financial implications may prevent routine analysis beyond the identification of the primary drug and adulterants.

The evidence for bacterial infections caused by illicit drug adulteration presented here is based on case study reports. The case reports are limited as they often draw the conclusion that the infection is due to drug adulteration in the absence of a drug sample available for analysis. Additionally, in some cases, the serum of the individual may not be analysed for presence of adulterants and the diagnosis may have been based solely on patient symptoms and their response to treatment (for example, O'Sullivan and Mahon^[41]). However, despite these limitations, it is possible that many bacterial infections caused by illicit drug adulteration go unidentified and it may be frequently assumed that bacterial infection was caused by unsterile drug administration without further consideration or exploration of adulteration.

The lack of routine forensic analysis of illicit drugs (including identification of adulterants) and identification of the cause of adverse health effects amongst drug users impacts upon opportunities to provide accurate information to the public. Whilst routine information of illicit drug adulteration continues to be unstandardised and often unavailable, it is difficult to distinguish the public health consequences of the effects of adulterants from the consequences of using a drug.

Implications of findings

This review provides an overview of drug adulteration patterns and the potential reasons why particular substances are used as illicit drug adulterants. The findings indicate that much drug adulteration typically involves substances which are legal, readily available, and likely to have minimal impact on users' health at low dosages. Other adulterants are used to enhance, mimic, or facilitate drug use. Improved awareness and information availability of adulteration patterns is required amongst drug users and those who are involved in the healthcare of drug users (including drug treatment practitioners, and emergency and community healthcare workers). Whilst many countries routinely collect data about the adulteration of illicit drug samples seized in their country, much of this data is not routinely reported. The UNODC has called for an early-warning system to identify new emerging drugs, which includes precursors and adulterants.^[1] The European Early-Warning System (EWS) for emerging drugs and emerging drugs trends identifies new and synthetic drugs, new trends in existing

drugs, and cases of counterfeit drugs (i.e. substances sold as drugs which do not contain any of the active ingredient). [42] The EWS is an effective model of sharing intelligence across Europe and internationally, where appropriate. However, the EWS is focused on new drugs, with trends in existing drugs and adulterants forming an additional section in reporting. Building on the EWS, an international early-warning system with an increased emphasis on adulterants of *all* illicit drugs (both existing and emerging) and rapid reporting of adverse effects could be the most effective method of monitoring, reporting, and reducing the public health consequences of this issue.

There is a need to understand the decisions made at all levels of the drug trade, from mass producers to street dealers, in order to fully understand and monitor drug adulteration practices. We recommend multimethods surveillance and monitoring of illicit drug adulteration and contamination in order to gain an accurate picture of the situation, including: testing of illicit drug products; qualitative analysis with drug users; assessment of production techniques; examination of the prevalence of drug use; and analysis of emerging drugs (such as legal highs). Collection of data should be standardised, but adapted to the source (for example, health service, coroner, poison control centre, drug treatment agency) and fed into a common database of shared intelligence across Europe and internationally.

Conclusion

The evidence suggests that illicit drugs are more commonly adulterated with: benign substances (such as sugars); those that enhance or mimic the effects of illicit drug (such as paracetamol in heroin); those that facilitate the administration of illicit drugs (such as caffeine in heroin which facilitates smoking); or as the result of poor or unsterile manufacturing techniques. Multimethods surveillance and monitoring of illicit drug adulteration and contamination are required in order to gain an accurate picture of adulteration practices and provide appropriate health responses and harm reduction.

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