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Review

Counterfeit Drug Investigations: Techniques, Challenges, and the Role of Abductive Reasoning

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ABSTRACT: Variable types of investigations exist regarding counterfeit drug detection, disruption, and regulation. Counterfeit drugs are spurious drugs, falsely labelled, falsified, substandard, unregistered/unlicensed, and infringe trademarks. Counterfeit drugs can mimic both legitimate and illegitimate drugs and are often distributed in virtual environments, such as illicit online pharmacies, the surface web, and the dark web. Counterfeit drug operators and operations are the typically corrupt and/or criminal individuals, groups, and techniques by which counterfeit drugs are produced and distributed. The manufacture and distribution of counterfeit drugs are ever-changing, which results in the need for investigative techniques that are equally adaptable and collaborative. Counterfeit drug investigations can be defined according to four categories: medical investigations in hospitals and through autopsies, chemical and non-chemical drug investigations in forensic toxicology laboratories, various track-and-trace technologies used in pharmaceutical industry investigations, and national and global coordinated investigations. Due to the diverse counterfeit drug investigations present, the logic and practice of abduction are highlighted as a primary part of the investigative element to counter ongoing efforts by offenders to evade detection. Abductive rationalities are prioritized in that they are contrary to an increasing reliance on technoscientific modes of data production alone. Rather, abductive reasoning plays a central role in counterfeit drug investigations at the levels of instigating and directing investigations, as well as interpreting and responding to evidential findings.

Keywords: Counterfeit drugs; Investigations; Forensic toxicology; Pharmaceutical industry; Criminal networks; Corruption; Abductive logic

1. Introduction

Variable types of investigations exist regarding counterfeit drug detection, disruption, and regulation. One primary area in which counterfeit drugs are associated is the pharmaceutical sector, which is a multi-billion dollar industry with various global sales estimated. A significant segment of the global pharmaceutical industry includes counterfeit drugs in medicines and pharmaceuticals. Counterfeit drugs are drugs that may be spurious, falsely labelled, falsified, substandard, unregistered/unlicensed, and infringe trademarks. They are typically inferior in terms of quality, safety and efficacy. They may contain little, inactive, impure, expired, or wrong ingredients, fake chemicals and packaging, and improper quantities [1], potentially damaging the pharmaceutical sector's reputation. The presence and continuing emergence of the counterfeit drug phenomenon exist in both material (*i.e.*, the streets, hospitals) and virtual sites (*i.e.*, online illegal pharmacies, the surface and dark webs), and by multiple counterfeit drug operators and operations. Many of the consumers are not aware of the circulation of counterfeit drugs, which leads to serious health repercussions, including death [2].

This review seeks to consolidate these diverse investigative approaches through the logic and practice of human-based abductive reasoning. Abductive processes are necessary throughout the investigative process, but particularly to initially instigate and guide counterfeit drug investigations, as well as to synthesize, interpret, and respond to the technoscientific evidential outcomes produced. As such, there are three key objectives to this study. The first objective is to provide a background and outline of the counterfeit drug phenomenon, including the types of drugs and the counterfeit operators and operations used to produce and distribute drugs. At this level, the internet provides an increasingly viable option for distributing counterfeit drugs, both legitimate and illegitimate, to domestic and

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international consumers [3]. A significant focus is dedicated to the supply of counterfeit drugs in virtual environments, with specific attention to illicit online pharmacies and other avenues for distribution through the surface and dark web (*i.e.*, social media, email, and online markets). Counterfeit drug operators and operations are the individuals, groups and techniques by which counterfeit drugs are produced, distributed and sold. There are two broad categories of counterfeit drug operators: informal and organized criminal networks, and 'grey areas', which include corruption that may exist in pharmaceutical industries as it overlaps with criminal involvement. Counterfeit drug operations refer to the specific techniques and procedures used to make these drugs.

The second objective, which is of primary importance, is to elucidate multiple investigative approaches, including forensic medical, forensic toxicological, pharmaceutical, and coordinated approaches. Forensic medical investigations occur in hospitals and morgues, forensic toxicological investigations interrogate the chemical and non-chemical nature of counterfeit drug make-up, pharmaceutical investigations involve multiple track-and-trace procedures, including blockchain and AI methods, while coordinated counterfeit drug investigations amalgamate the first three approaches in national and global contexts. There are similarities and distinctions between these four methods. The complexity associated with all four investigative types, however, reveals how the creation and delivery of counterfeit drugs are ever-changing (*i.e.*, through the production of drug analogues and derivatives), which results in the need for investigative techniques that are equally advanced and collaborative across multiple domains.

The third objective is to re-prioritize the role of human thought processes in investigative contexts, particularly those of abductive and digital abductive modes of reasoning, as these may translate into methods and practices. Drawing attention to abductive logic is essential in the counterfeit drug investigative context as it is otherwise largely dominated by techno-scientific methods that do not always act perfectly. Technoscientific methods may complement human reasoning in investigative situations but also present multiple challenges, confusions, and complexities. The related logics of abduction and digital abduction are thus presented as creative and open-ended rationalities that can mirror the equally inventive efforts by offenders to evade detection. Abduction is a useful logical process that contains generative reasoning to observe, identify, classify, interpret, and hypothesize counterfeit drug theorizing and evidence in both material and virtual domains.

2. The State of the Art (SOTA) Methodological Approach

Counterfeit drug investigations are complex and fluid and require an equally flexible methodological framework. Consequently, the state of the art (SOTA) literature review approach was chosen as it allows for multiple perspectives on a given topic [4]. It is a literature review that enables the synthesis of large bodies of knowledge, is particularly relevant to scientific information research, and facilitates decision-making in these knowledge spheres. Literature reviews support knowledge advancement in scientific and technological contexts by collecting, describing, analyzing and integrating large bodies of data and knowledge. The SOTA review approach rests on four propositions. First, the literature addressed should offer multiple perspectives on the topic, as different researchers may hold varying perceptions or interpretations of the data. Second, SOTA assumes that the phenomenon's reality cannot be completely perceived or understood due to limitations, such as the capabilities of current technologies. Here, the researcher conducting the literature review can only perceive a limited part of the phenomenon. Third, the phenomenon's reality is viewed as subjective and inter-subjective constructions. This means that conceptualizing a particular phenomenon is a construction by individual perceptions as this shapes given understandings. Finally, the overall argument and research objectives in which the review is conducted inform the review findings.

Based on these four propositions, the following review seeks to incorporate the research objectives and orientations relating to counterfeit drug investigations in synthesizing this discussion. This review contains the assumptions that reality is socially and experientially informed and no single objective truth exists. The research presented and interpreted is subject to changes over time and may conflict with alternate understandings in past and future contexts. As it relates to counterfeit drug investigations, this review is a subjectively informed summary and analysis of contemporary thinking on this topic. It seeks to contextualize contemporary depictions and understandings of counterfeit drug investigations and presents an argument about how literature may be interpreted. The emphasis is on exploring the historical shaping of counterfeit drug approaches, the factors that inform changes in understanding, and the ways of thinking that could inform further insights.

The primary emphasis is on counterfeit drug investigations but also incorporates perspectives that diversify and extend this knowledge, including potential emerging and future directions. The SOTA approach is, therefore, unique in that it is inherently different from other forms of knowledge synthesis in presenting broader perspectives as they relate

to and enhance understanding of counterfeit drug investigation knowledge development. In all, the review focuses on the data that is currently available, the nature of that data, and potential gaps in the knowledge [4]. Prior to acknowledging the complexities associated with counterfeit drug investigations, a broader look at the counterfeit drug situation, the actors involved in producing such drugs, and the environments and techniques by which they are distributed is considered.

3. The Counterfeit Drug Phenomenon

The pharmaceutical sector is a multi-billion dollar industry with estimated global sales. In one estimate, the global pharmaceutical market will exceed $1.5 trillion United States dollar (USD) in 2023. It will continue to grow by a 3–6% compound annual growth rate in the following five years [5]. Other research has found that counterfeit drugs annual markets range from US $70 to $200 billion [6]. Growth is seen as being driven by the United States, which is expected to account for 40% of the market by 2023. Growth in emerging markets is also expected to be strong, with sales in China approaching the combined sales of the five major European markets (France, Germany, Italy, Spain, and the United Kingdom) by 2023 [3].

A significant segment of the global pharmaceutical industry includes numerous types of counterfeit medicines, pharmaceuticals and/or illegal imitation drugs. Counterfeit drugs include those that may be spurious, falsely labelled, falsified, substandard, unregistered/unlicensed, and infringe trademarks. For example, substandard medications are authorized medical products that fail to meet quality standards or specifications. Unregistered and/or unlicensed drugs are medical products that have not undergone evaluation and/or approval by the national or regional regulatory authority for the market from which they originate. Falsified drugs are medical products that deliberately/fraudulently misrepresent their identity, composition, or source [3]. They are typically inferior in terms of quality, safety and efficacy. They may contain little, inactive, impure, expired, or wrong ingredients, fake packaging, and improper quantities [1]. Counterfeit drug classifications can be broadly divided into those that mimic authentic drugs (*i.e.*, falsified, substandard and generic drugs), and those that mimic illegal drugs. Counterfeit drugs in the legitimate realm include painkillers, cancer, lifestyle medications (*i.e.*, cosmetic), contraceptives and fertility treatments, diabetes, heart, HIV and hepatitis, malaria, psychotropics, vaccines, anti-epileptic, and antihistamines [3]. Counterfeit illicit drugs include stimulants (cocaine, methamphetamine, and other amphetamines), narcotic painkillers and opioids (oxycodone, fentanyl, morphine, codeine, and methadone), and sedatives (barbiturates and benzodiazepines) [1]. As such, there is a breadth, complexity, and diversity associated with counterfeit drug classifications, definitions, and examples, which relate to, and extend beyond, the global pharmaceutical industry.

In efforts to evade detection and legal repercussions, counterfeit drug producers and suppliers can reformulate the chemistry associated with both legitimate and illicitly mimicked drugs. New chemical structures are produced and are constantly changing in attempts to stay ahead of the laws that prohibit such drug use (*i.e.*, the creation of synthetic cocaine) [7]. For example, increasingly complex counterfeit drug manifestations arise in the form of new psychoactive substances, which are labelled as a range of drugs that have been designed to mimic established illicit drugs, such as cannabis, cocaine, methamphetamines, and LSD [7]. Regarding fentanyl, for example, this drug and its analogues have been created and diverted away from their original medicinal purpose to being manufactured in clandestine laboratories for the illicit drug market. These derivatives have a chemical structure like, but not the same as fentanyl, and have been developed to bypass toxicological screens and laws banning illicit substances.

The Geographical Contexts of Counterfeit Drugs

The prevalence of counterfeit drugs is an international phenomenon. Counterfeit drugs have been found in 124 countries across all continents [3]. This is due to globalization, trade facilitation, and the rising economic importance of intellectual property as key drivers of economic growth. Challenges exist in governing the counterfeit drug trade in all countries, but are particularly prevalent in developing countries, where the informal distribution of counterfeit drugs is more widespread and less secure. The World Health Organization (WHO) reported in 2017 that an estimated one in ten medical products circulating in lower and middle-income countries (LMICs) is either substandard or falsified [8]. Many of these counterfeit medications came from India, with Germany, Singapore, the United States, Canada, and the United Kingdom also mentioned [3].

Counterfeit drugs also contribute to a significant global death toll. An older estimate from the World Health Organization (WHO) puts the annual global death toll from counterfeit drugs at around one million [6]. Counterfeit drug-related deaths have been specifically reported, but are not limited to, the United States, Canada, and Europe

(mostly Sweden, but Hungary, Belgium, Switzerland, Poland, UK, and Germany) [9]. The basis for death varies in relation to counterfeit drugs. In several cases, death is attributed to counterfeit non-prescription Tylenol, vaccines, oxycodone, new psychoactive substances, and illicit opioids, particularly fentanyl and its derivatives/analogues. In the United States, approximately 75% of drug overdose deaths in 2020 involved opioids [10]. In addition to the consequence of death from counterfeit drugs, other types of life-threatening complications and adverse effects exist, including the failures of treatments and cures, resistance to drug therapy, the increased risk of prolonged illnesses, and the increased severity and complications in health symptoms [7]. Many of these complications, such as resistance to drug therapies, have been identified specifically in the cases of pneumonia and malaria-related deaths [3].

This global picture of the counterfeit drug phenomenon can be further broken down into specific regions. In North America, substantial literature is dedicated to the United States (US). Several important drug-related epidemics have been occurring in the US since the 1970s until today [9]. A large portion of the counterfeit drug issue in the US is limited to specific populations and types of drugs, such as drug-users exposed to counterfeit fentanyl-laced oxycodone tablets and adult men exposed to counterfeit lifestyle drugs like sildenafil citrate. This is a much different situation than in other parts of the world, where the risk posed by counterfeit drugs to populations is more often related to the treatment of deadly diseases [8]. The Asia-Pacific, Central and South America, Europe, and Africa are other regions of the world where counterfeit drugs are present and emerging. Traditionally, the biggest producers of counterfeit drugs are China, India and Russia. India remains a significant producer of counterfeit pharmaceuticals. In Central and South America, there has been an increase in the number of pharmaceutical crimes [9]. Relatedly, a large group of counterfeit drug consumers has been found in Africa, where approximately 200,000 people are said to die each year due to fake antimalarial drugs. Estimates of the prevalence of counterfeit drugs in some parts of Africa and Asia reach as high as 70% [7]. Importantly, how counterfeit drugs become available for public consumption in national and global contexts varies in some ways. However, the increasingly prevalent use of virtual environments to distribute counterfeit drugs, such as online pharmacies, renders the acquisition of these drugs relatively simple and leads to an increasing ease by which such drugs are acquired.

4. Online Pharmacies and Related Virtual Environments

The internet is an increasingly viable option for distributing pharmaceutical products, both legitimate and illegitimate, to domestic and international consumers [3]. The supply of counterfeit drugs is often distributed in virtual environments, with a specific emphasis on online pharmacies. Online or digital pharmacies are Internet-based vendors (legal or illegal), typically selling medicines, sometimes called ‘cybermedicine’ [11]. Online pharmacies have existed for decades, but the global COVID-19 pandemic saw a surge in use due to convenience and cost [12]. The pandemic led to an exponential growth in the number of online pharmacies. Financial motives, convenience, and discretion were cited as the main motives for buying pharmaceuticals online [13]. Online drug purchases further appeal to consumers due to the speed and convenience of purchases; lower costs; the ability to avoid discussing sensitive conditions with healthcare professionals, family, employers and/or authorities; and the frequent absence of a need for a prescription [3].

There are typically three types of legal online pharmacies: traditional pharmacy sites, which dispense a prescription drug only after the submission of a legal prescription order; prescribing-based sites, which provide prescriptions to patients after online or phone interactions; and, online drug shops, which sell prescription drugs after consumers indicate what drugs they wish to purchase online [11]. In 2015, the estimated number of online pharmacies was approximately 30,000 to 35,000, with an additional 600 launching each month [3]. Of these approximately 35,000 online pharmacies worldwide, 95% to 97% are said to be operating in varying degrees of illegality, and approximately 92% are operating illegally in a blatant manner. The transition and overlap between legal online pharmacies transcending into illegal or ‘rogue’ pharmacies is a frequent occurrence. An illegal online pharmacy is defined as failing to meet national and international pharmacy regulations and/or not being subjected to the requisite regulatory review, licensure and/or certification. Online illicit pharmacies occur by violating state, provincial and/or federal law, the relevant pharmacy standards, and/or failing to adhere to applicable legal requirements [3]. Counterfeit drugs are largely sold in rogue online pharmacies [14]. The World Health Organization (WHO) estimates that 50% of drugs for sale on the Internet are counterfeit and that drug counterfeiters are taking advantage of the rising ‘self-prescribing culture’ [3].

The internet can further be divided into the surface (open) web and the dark (deep) web, of which counterfeit drug distribution and purchasing varies. At the surface web level, there has been an increasing growth of opportunities for counterfeit drug operators to sell illicit drugs. The surface web enables diverse online platforms to reach potential customers beyond online pharmacies. These include social media and direct solicitations to potential customers using

email and online advertising. Detecting counterfeit drug operations and networks is difficult at the surface web level due to the ease by which new websites can be established, the high level of anonymity offered in the virtual world, and the difficulties for security and law enforcement personnel to identify and make associations between diverse and wide-ranging counterfeit drug networks [3]. This is often because the surface web transcends national boundaries and, thus, national laws, jurisdictions, and legal controls [13]. Counterfeit drug operators have often developed sophisticated techniques to evade detection on the surface web.

The capacity to evade detection is heightened in dark and deep web environments. Dark markets, which are concurrent with the dark web, are online shopping platforms that reflect a highly anonymized part of the internet that is not indexed by traditional search engines. The dark web does not have the same types of formal guardians as the surface web. These dark markets facilitate new ways of trading and openly selling illicit and/or counterfeit drugs and other fraudulent products. Many of the drugs listed and sold on the dark web are illegal drugs, which account for 60–80% of all listings [15]. Relatedly, many drug chemicals and compounds can be purchased and received anonymously on the dark web, to manufacture counterfeit and other illegal drugs [9]. Further related counterfeit products and services available on the dark web, include access to vaccines and medicines, hacking services, weapons, guides on how to defraud people, and others. The dark web operates similarly to the surface web in the sense that products are sold, and buyers can leave reviews [15]. Distributing counterfeit drugs in virtual environments requires substantial and sophisticated knowledge about how to create and produce such drugs. The offenders responsible for drug development and distribution are typically categorized as either 'criminal' or 'corrupt', depending on the precise geographical location in which they are located, affiliation to a criminal network, technoscientific methods used, and the potential relationship to the pharmaceutical sector.

5. Counterfeit Drug Operators and Operations

Counterfeit drug operators and operations, for the purpose of this discussion, refer to those individuals, groups and institutions that produce, manufacture and distribute counterfeit drugs (operators), including the specific techniques and procedures used (operations). There are two broad categories of counterfeit drug operators. The first ranges from informal to more organized criminal networks, and the second is 'grey areas', which include corruption that may exist in pharmaceutical industries as it overlaps with criminal involvement. There is not always a clear distinction between these two categories. Informal and more organized crime networks are often transnational in nature and use variable methods, including clandestine laboratories and illicit online pharmacies, to manufacture and distribute counterfeit drugs and medicines [3]. The ability of counterfeit drug distributors to use deception, hide their identity, and misrepresent drug products through online pharmacies, surface and dark web environments is attractive as these virtual contexts provide a relatively easy point of entry into otherwise regulated markets. Criminal involvement in the manufacture and distribution of counterfeit drugs often provides substantial profits to support other illicit activities, such as money laundering, human trafficking for sexual exploitation, and weapons smuggling [3].

The second type of counterfeit drug operators is deemed 'grey areas'. This refers to corruption within the legitimate pharmaceutical industry community and a lack of resources dedicated to law enforcement agencies to govern this issue comprehensively [16]. Corruption may manifest when legitimate pharmaceutical drugs cross the borders of various countries, and numerous importers, retailers, and distributors, including criminals, gain access. Corruption in the supply chain is exacerbated by drugs being delivered almost 100% of the time through postal services. Postal methods for transporting counterfeit drugs are a key vulnerability as postal information is typically only available to customs officials in paper form at the time of importation and is easily incorrect [3]. These corruption scenarios create overlaps between what is often presented as dichotomies of licit/illicit, online/offline, and local/global. A sub-section of the pharmaceutical industry is pseudo-legitimate pharmaceutical companies that facilitate the counterfeit drug trade more easily. These pseudo-legitimate companies attempt to operate under the guise of a legitimate company, which provides a front to sell counterfeit drugs for extra income and launder profits, as these methods overlap with criminal networks [17].

Counterfeit drug operations are how drug operators conduct their business. Counterfeit drug operations often occur due to the connection between the legal/illegal and legitimate/illegitimate manufacturers and suppliers of counterfeit drugs. The first type of counterfeit drug operation relates to supply chains. Supply chains are the marketing, transport and distribution of pharmaceutical products and medicines into supply channels. Counterfeiter drug operators succeed in this way by exploiting weaknesses in supply chains, which are often fragmented. The continuous variation in marketers, transporters, and distributors can make detecting and identifying counterfeit drug origins difficult. Counterfeit drug operators gain access to supply chains primarily through second-tier distributors, which are less heavily

monitored and regulated [3]. This lack of oversight, predominantly in the second-tier distribution environment, enables corruption vulnerabilities in the pharmaceutical industry that are present throughout the distribution chain. At any point where there is a lack of oversight, drugs, and medicines can be stolen and sold on the black market, which is a high risk in many countries. Weaknesses in the supply chain create opportunities for criminal networks to expand the scope and scale of their operations, including manipulating intellectual property rights and national and international trade routes to disguise and transport counterfeit drugs.

Other areas of counterfeit operations include packaging and repackaging, illegal diversion and theft. Counterfeit drug operators engage in deceptive practices, including marketing counterfeit drugs as legitimate medicines. The operators will package and repackage counterfeit drugs in a way that mirrors genuine medicines. Repackaging can undermine the integrity and therapeutic benefit of legitimate medicines, and counters anti-counterfeiting techniques, such as product tracking mechanisms used by pharmaceutical companies. Detection of counterfeits requires expert examination, which can be costly [3]. Illegal diversion and theft are techniques that facilitates the availability of counterfeit drugs. Illegal diversion occurs when a genuine pharmaceutical drug is approved and intended for sale in one country, but is illegally intercepted and sold in another country [18]. This enables the concurrent effect of the transition of legitimate medicines intended for consumers in a regulated market to their presence in an unregulated market.

At the transnational level, illegal diversion often occurs using false statements and declarations in border and customs contexts regarding the false status of counterfeit and falsified drugs as they are made to look legitimate [3]. The related pharmaceutical theft involves burglary, robbery, or the embezzlement of drugs. The criminal/corruption interconnection is often apparent here as thefts are coordinated between pharmaceutical employees and professional criminals. The theft of pharmaceutical medicines and drugs may occur anywhere in the supply chain, including the manufacturing site, freight forwarders, distribution centers, warehouses, pharmacies, and hospitals [3]. The facts regarding what counterfeit drugs are; the often virtual environments they exist in and are sold; the individuals, groups and institutions responsible for their manufacture; and the techniques used to distribute are a necessary background and context to comprehend the investigative environments and strategies used to detect and identify counterfeit drugs. This overview so far elucidates the complicated nature of digital, technological and scientific knowledge required for these drug productions and distributions. Likewise, the contemporary investigative strategies used to identify counterfeit drugs and translate this knowledge into evidence are equally technoscientific.

6. Current Investigative Approaches

In the current global context, counterfeit drug investigations can broadly be defined according to four categories. The first category is medical investigations that seek to identify counterfeit drugs in bodies and bodily matter, typically in emergency departments and in postmortem forensic toxicology environments. Hospital-based investigations usually take place in emergency departments and assess overdosed individuals, and postmortem forensic toxicology investigations use autopsies to analyze drugs in bodily material after death has occurred. The second category is chemical and non-chemical forensic investigations that analyze counterfeit drug materials as separate from human ingestion. Forensic toxicological analysis in this context takes place in a crime laboratory or at a field site (*i.e.*, crime scene or scene of death). The third category is pharmaceutical industry investigations, including security measures taken, to deal with many facets of drug creation, manufacturing, and distribution processes related to counterfeit drugs. The final category includes coordinated counterfeit drug investigations and responses, which deal with multiple actors across the investigative, prevention and response fields. Within all four investigative contexts, some challenges stem from the chemical composition of the drugs, their existence in operational and virtual realms, and the multiple players involved in their manufacture, production, and supply.

6.1. Medical Investigations

Forensic medicine is the application of medical knowledge to law enforcement, criminal investigation, and the legal system. Toxicology in this context is the study of the adverse effects of chemicals on bodily matter and human health. Medical investigations assess counterfeit drugs after they have been ingested and are, thus, part of an individual's bodily matter. Medical investigations into counterfeit drugs can take two forms: often related and interchangeable. These investigations occur in the dual contexts of hospital (emergency) and postmortem toxicological (autopsy) settings.

6.1.1. Hospital Investigations

Toxicological analyses in a hospital setting usually occur in an emergency department. Medical investigations, here, are aimed at overdosed individuals who may be still living, near death, or transitioning to death. The hospital investigation tests bodily matter to determine the types and levels of illicit drugs present. Emerging and priority counterfeit drugs in many emergency departments relate to fentanyl, oxycodone, hydrocodone, alprazolam, stimulants (*i.e.*, cocaine), as well as mixtures between these, such as heroin and synthetic opioids. Fentanyl is prevalent within the counterfeit drug markets, with most fentanyl analogues not having been developed and approved as legitimate medical and pharmaceutical products [9].

Emergency doctors can detect signs of a potential opioid overdose as they are often like those caused by heroin and fentanyl (*i.e.*, morphine, hydrocodone, oxycodone, hydromorphine, and methadone). The immediate overdose symptoms include euphoria, drowsiness, dizziness, confusion, pinpoint pupils, skin rash, nausea, vomiting, constipation, sedation, tolerance, addiction, bradycardia, respiratory depression, unconsciousness, coma and death [9]. The addictive, euphoric effects produced by fentanyl, synthetic opioids, and related drugs are linked to the activation of the u-opioid receptor in the brain. A key, recurring symptom that often leads an individual to transition from an overdose state to death, is respiratory depression [10]. A related condition that may occur over longer periods of time includes, but is not limited to, hepatitis, which is liver inflammation [1]. Overdoses and fatalities have also been reported with legitimately prescribed and therapeutic uses of fentanyl and other opioid-based drugs [9].

The types of techno-scientific procedures used in emergency department settings to detect counterfeit and other illicit drugs include, as one example, magnetic resonance imaging studies. The types of bodily materials analyzed for counterfeit drug levels in this manner include blood concentrations (peripheral blood and white blood cell counts); creatinine levels (to check how well kidneys are filtering blood); hepatic, aspartate and alanine aminotransferase concentrations (primarily to check liver health); and troponin concentration (to check heart health). These toxicology studies are done to determine if there are drug-related conditions such as leukocytosis (a high white blood cell count), renal insufficiency (poor kidney functioning, often due to reduced blood flow to the kidneys), rhabdomyolysis (muscle breakdown), and compression neuropathy (unusual pressure on a peripheral nerve, connected to the brain and spinal cord) [19].

An example of a hospital-based counterfeit drug investigation took place in one American hospital during the period of 2017–2022. This investigation used counterfeit pill investigative data that was reported to the Toxicology Investigators Consortium (ToxIC) core registry that is part of this hospital. The registry includes data from bedside consultations (*i.e.*, patient or proxy interviews, physical examination, and ancillary data). Variables collected include patient demographic data characteristics, exposures (*i.e.*, types of drugs taken), clinical presentation (*i.e.*, respiratory depression), treatment administration (*i.e.*, naloxone), and outcomes (*i.e.*, hospitalization) [20]. Cases in the ToxIC core registry were identified as those in which the medical record mentioned the use of suspected counterfeit M-30 oxycodone, symptomatic exposure to fentanyl (*i.e.*, acute opioid overdose) or acute withdrawal from fentanyl, and administration route not typical for prescription fentanyl (*i.e.*, nondermal) [20].

There were 986 counterfeit drug cases initially identified. However, only 481 were selected (48.8%) due to the relevant factors associated with exposure and acute withdrawal symptoms, routes of administration, and clinical signs and outcomes. Many of these cases related to the suspected counterfeit M-30 oxycodone drug, with 143 of these exposures admitted to hospital and 209 experiencing acute withdrawals. Patients with exposures were predominantly male (143 or 71.3%). Among exposures, the most reported routes of administration were ingestion (44 or 31.2%) and inhalation (36 or 25.5%). Of the 143 patients with exposures, the majority were hospitalized (116 or 81.1%), and 80 of these patients were admitted to an intensive care unit (69%). Among patients with exposures, 74.1% had clinical signs of an opioid toxidrome, 56.6% had respiratory depression or bradypnea, and 38.5% had coma or central nervous system depression. There were two deaths from patients with exposures (1.4%). The most detected substances co-existing with oxycodone and fentanyl were amphetamine/methamphetamine, benzodiazepines, and cocaine [20].

These findings reveal that persons who ingest counterfeit drugs may believe they are using legitimate prescription drugs. Other reports suggest that persons using such drugs might be shifting from using traditional opioids to intentionally ingesting counterfeit drugs because of cost, convenience, difficulties with injection, and reduced stigma. This study found that detection of substances other than fentanyl is common. It also found that co-exposure can mask opioid-related signs and complicate treatment. Approximately two-thirds of exposures involved people aged 15–34 years. It was found that easy access to counterfeit pills through rogue online pharmacies, social media, and the dark web might be increasing exposure to counterfeit drugs and the subsequent increase in risk of overdose deaths [20].

6.1.2. Autopsy Investigations

The emergency department is typically focused on overdosed yet living individuals. Suppose a transition to death occurs in a hospital setting or an overdose-related death is found at a crime scene/scene of death. In that case, a second medical investigation, deemed forensic postmortem toxicology, is instituted. Forensic toxicology, in broad terms, is the branch of science that uses chemical or analytical techniques to investigate and identify any chemical and drug substances in humans related to investigative and judicial proceedings. More specifically, forensic postmortem toxicology investigations study bodies and bodily materials, in this case, counterfeit drugs, after death. These forensic medical experts are referred to interchangeably as medical examiners, coroners, and/or forensic pathologists. They undertake medical, investigative and laboratory studies to determine the cause and manner of death. A relationship is typically established by the forensic postmortem toxicologist between exposure to chemicals/drugs and an injurious effect causing death (*i.e.*, accident, suicide, overdose, homicide). These medical investigations try to determine whether counterfeit drugs were a cause or contribution to death, or if they caused impairment leading to death [21]. These investigators are located at crime scenes and/or morgues to identify and collect any further physical evidence items that may be useful in the investigation of the death (*i.e.*, drugs, packaging, and other related objects [19].

The bodily and material evidence recovered from a crime scene, death scene, and/or morgue informs the types of forensic postmortem toxicological tests conducted, typically in the form of autopsies [10]. The autopsy process aims to detect any alcohol, prescription medications, illicit and counterfeit drugs that are present in the postmortem biological samples of the deceased [19]. Multiple types of postmortem bodily fluids, tissues, organs, and samples can be measured. The most common investigations focus on urine and blood concentrations (serum, femoral vein blood, peripheral blood, heart blood, and central blood), vitreous humor, gastric contents, brain tissue, liver, bile, kidney (creatinine), adipose tissue (endocrine system), and spleen analyses [9,19]. In counterfeit drug-related autopsies, biological samples are often analyzed in terms of 'drug metabolites', which are a type of evidential biomarker. A drug metabolite is a compound that is formed in the body through the metabolism process of the drug. It relays information about the drug's efficacy or toxicity as it interacts with an individual's bodily functioning. Fentanyl and fentanyl analogues, for example, produce fentanyl-related metabolites in biological samples as biomarkers after consumption. They indicate drug consumption levels, particularly in acute intoxications and fatalities [9].

A 'postmortem positive result' is when a counterfeit or illicit drug is detected in the bodily samples of the deceased during the autopsy [10]. This result is confirmed when there are relatively clear indicators that a deceased has consumed a specific counterfeit or illicit drug. These drugs may also be identified by coroners, medical examiners, and forensic analysts, based on the presence of alternative or unknown substances detected in bodily samples or fluids [7]. Indicators that counterfeit drugs are present in a deceased can also be determined by drugs found in the deceased that do not match their medication lists, prescriptions, or pills in their possession. If there is uncertainty regarding the type of drug found in the autopsy, medical investigators can request further chemistry studies, including the analysis of suspicious illicit tablets found at the scene of death [19].

6.1.3. Artificial Intelligence (AI) in Forensic Medical Investigations

In addition to more traditional medical approaches to autopsies, artificial intelligence (AI) is increasingly incorporated into these medical assessments and procedures. The traditional way of doing an autopsy has many limitations, for example, it requires experienced human engagement in every case and some smaller observations can be missed by a visual examination alone. These limitations have justified the use of advanced technology, such as AI, in the autopsy settings [22].

AI is one technological advancement and refers to the possibility that machines can simulate human functioning and thought processes [23]. AI is a discipline that combines computer science and data sets to enable problem solving. It also encompasses the subcategories of machine learning and deep learning, which are often mentioned alongside AI. These disciplines comprise AI algorithms that seek to create expert systems that make predictions or classifications based on input data. These disciplines have made significant advances in the various domains of forensic science, as they can connect various databases and other sources of information in the investigative process. This often occurs across disciplines to link current and past crimes [24]. AI in forensic medicine and pathology includes building smart machines that can perform tasks like human intelligence as it relates to assessing post-mortem interval (PMI) estimation, personal identification, and tissue/fluid identification [22]. Recently, AI technologies have opened new perspectives in forensic contexts by analyzing big data and creating new prediction models to form accurate, rapid and uniform opinions related to forensic case examination. This typically occurs by comparing the data from investigator findings with the

data available from machines [22]. AI works in conjunction with medical experts to complement their analysis of post-mortem changes of microorganisms in different organs/tissues at various taxonomic levels [23].

AI is used at the level of postmortem medical technologies. Currently, there are various methods for chemical and bodily forensic toxicological procedures. These include photo spectrometers, chromatography, neutron activation analysis, and high-performance liquid chromatography. These are advanced techniques, but human error can result in the wrong analysis of samples. AI has been implemented in machine contexts to improve the analysis of samples and in a less time-consuming way. AI can also be combined with robotics to automate some aspects of toxicology testing, such as collecting and transporting samples [22]. One example of this is Omics data mining. Omics is the suffix used in various branches of biology, such as genomics, proteonomics, metabolomics, and toxicogenomics. Omics technologies involve a large amount of scientific data, which can be utilized in the forensic field for the calculation of postmortem intervals, diagnosis of disease, and analysis of drug abuse and poisoning cases. In this context, Omics technologies produce large amounts of data regarding gene expression, protein measurement, metabolite levels, and microbial interactions. Omics data can be integrated with AI through machine learning tools to detect various evidential biomarkers in forensic medical environments [22].

6.1.4. Counterfeit Drug Detection in Autopsies

Medical postmortem forensic investigations pertaining to counterfeit drugs are complex. In one study, postmortem cases were screened for counterfeit pharmaceuticals and other illicit drugs using liquid chromatography/orbitrap mass spectrometry [25]. Further investigation of cause/manner of death occurred, if deemed necessary, through untargeted gas chromatography/mass spectrometry with nitrogen phosphorous detection and a novel, emerging drug screen via orbitrap high-resolution mass spectrometry. Toxicologically positive substances from these screening techniques were generally confirmed with quantitative liquid chromatography/tripole quadrupole mass spectrometry. This study occurred in the North Carolina Office of the Chief Medical Examiner (NC OCME) toxicology unit, which received nearly 13,000 counterfeit drug case submissions in 2020, nearly 15,000 in 2021, and just over 15,000 in 2022, for a total of almost 43,000 case submissions in this three-year period. Cases were designated to be appropriate for analysis whenever data and/or case history indicated the possible involvement of counterfeit pills in a deceased, as was identified during toxicology analysis, analytical batch review, and administrative review [25]. In total, a sample of 75 postmortem cases were extracted from the NC OCME toxicology unit based on personalized characteristics and toxicological data related to suspected counterfeit pill-involved deaths in this timeframe. Cases were selected for inclusion if observed to have a strong case history, such as direct bystander observation of pill consumption, remaining pills observed or collected at the scene, text message history, and/or friend/family account detailing recent pharmaceutical pill purchase [25].

Alprazolam and oxycodone were the primary drugs presumed to be counterfeited in this dataset, based on their reported consumption at the scene investigations and in toxicological results. Scene investigations refer to death scenes where medical examiners and law enforcement are responsible for documenting and collecting counterfeit drug-related evidence at the scene. The scene investigation includes detailed information about the drugs and/or paraphernalia found at the scene, which can yield valuable epidemiological information for understanding death trends. Scene information indicating drug type or class can help direct targeted toxicological analysis in an environment of limited resources. This is especially important where expanded toxicological surveillance testing is not possible for each deceased. Instances of counterfeit pill-involved deaths are typically under-counted in forensic medical investigations when pill material, evidence of purchase or bystander accounts are lacking.

Consequently, this investigation revealed a list of 86 compounds, including 16 common natural, synthetic and semi-synthetic opioids, as well as 35 psychoactive opioids, including fentanyl analogues. It also included 12 benzodiazepines, six stimulants such as methamphetamine and cocaine metabolites, six synthetic cannabinoids, and 11 additional substances such as gabapentin and PCP. It was found that cases indicative of counterfeit oxycodone consumption were more obvious, where investigatory information indicating possible counterfeit alprazolam consumption produced more varied postmortem findings, as the latter often co-existed with fentanyl and novel benzodiazepines. Medical examiner information indicated that the deceaseds obtained counterfeit medications from direct interpersonal relationships, the ‘street’ and online environments. Some case histories indicated that individuals may have been knowledgeable or suspicious of the counterfeit nature of the pills. Overall, this study was not meant to be comprehensive but rather include select examples of possible counterfeit pill-related deaths [25]. This section outlines how the autopsy is a medicolegal approach used to analyze the potential presence of counterfeit drug ingestion as inseparable from the bodily matter inherent to a deceased. However, there are forensic toxicological approaches that

seek to investigate counterfeit drug constitution at the level of the drug material itself, including chemical composition. These investigative practices are often related, yet require slightly different investigative rationalities, practices and settings.

6.2. Drug Investigations

Analyzing the counterfeit drugs/medicines/pharmaceuticals themselves is a related form of forensic toxicological investigation that focuses on the drugs as separate from ingestion by a living being. Toxicology, in this situation, can be characterized by analytical methods that are constantly updated to keep up with new analytical trends. These trends require constant development of novel analytical tools, including efficient sampling procedures, appropriate sample preparation protocols, and suitable methods to optimize the detection of compounds even at trace levels [24]. These investigations can traditionally be classified into two categories: first, as field methods (*i.e.*, at a sample site or crime scene) using portable devices; and second, in the laboratory using benchtop analytical instruments, as this usually relates to drug sample collection, storage, transport, and verification from the field. The field testing of potential counterfeit samples is different from laboratory work in that the latter is typically intended to provide confirmation and additional testing of field results to support investigative and adjudicative actions through the production of evidence [8].

6.2.1. Traditional Field and Laboratory Investigations

Field screening methods for the detection of counterfeit pharmaceuticals at the sample site have been extensively deployed, and a large range of tactics exist. The crime scene, sample site, and field testing will be considered synonymously for the purpose of this discussion. Field laboratory instrumentation seeks primarily to uncover the chemical constitution of drugs. A few common types of portable technologies include ultra-high-performance liquid chromatography, gas chromatography-mass spectrometry (GC-MS), color tests, paper chromatography, thin-liquid chromatography, mid-infrared spectroscopy (mid-IR) and Raman spectroscopy. In all, chemical field-testing methods are generally chromatographic and/or spectroscopic [8]. Field testing provides a type of initial surveillance of the drug, as opposed to the formal laboratory, which can conduct more sophisticated investigations. Field instruments seek to generate comparative results that compare the suspect counterfeit drug sample with the equivalent drug produced by a legitimate pharmaceutical manufacturer. If significant differences between the two samples are detected, a suspect drug can be removed from the supply chain as quickly as possible. Therefore, field analysis aims to enable a rapid response, remove counterfeit and/or dangerous materials immediately, and reduce the burdens on laboratories, where toxicological laboratory analysis may require considerable time and expertise [8].

Forensic toxicology in the laboratory is closely related to toxicological field testing of counterfeit drugs. The toxicological field testing takes place at a crime scene or ‘sample site’, and the forensic toxicology laboratory testing will typically be performed to confirm preliminary identifications of screening results from the field, both through chemical and non-chemical analysis. The ability to detect and identify counterfeit drugs, whether in the field or the forensic toxicology laboratory, is also dependent upon the ability to differentiate the suspect sample from the authentic version. This comparison informs about the ‘history’ of the suspected counterfeit drug sample [8]. The analysis of potential counterfeit drug’s chemical composition is central to field and laboratory investigations of forensic toxicological procedures to perform physical and chemical characterizations of the suspect drug. This includes identifying and extracting chemical composition and disintegration, color, physical properties, and the amount of active ingredients and impurities present [7]. The chemicals inherent to counterfeit drugs are potentially very complex and variable.

Non-chemical counterfeit drug testing may involve analysis of drug-associated features, such as packaging, that is related to a suspect sample and may provide further information. These typically involve visual indicators that a drug is not authentic, such as assessing its color, dimensions, and shape. Forensic crime and pharmaceutical toxicology drug investigators converge at the point that they are both keen to maintain secrecy regarding their anti-counterfeiting drug methods. This is a deliberate strategy to minimize the ability of counterfeit drug operators to understand their modes of investigation, as knowledge of their investigative tactics could facilitate better-informed counterfeit drug operations [8].

6.2.2. Forensic Toxicology and Artificial Intelligence (AI)

In addition to the aforementioned techniques, AI in toxicology improves the reliability and speed of testing. It is also useful for identifying new psychoactive substances and understanding the functioning of molecules that can be used in emerging drug formations [23]. Recently, AI algorithms have been developed to prevent the development of new counterfeit and illicit drugs. An example is DarkNPS, which can produce 8.9 million drug compounds that modifications of existing drug molecules could potentially create. DarkNPS works like a human brain to understand a

chemical sequence [24]. Another example is the product RXScanner, developed by RXAII, which is a device powered by AI and machine learning technology that can authenticate medicine for quality in approximately 30 s. To date, over 100,000 doses of counterfeit drugs have been removed using this product from supply chains in Africa and Southeast Asia [26]. However, there are limits to AI in forensic toxicology, including costs, the scarcity of data available, and the legal value of the data analyzed and reported by AI. Therefore, the human expert's role is still essential who in defining and more appropriately attributing the data analyzed to the specific drug case [23].

6.2.3. Counterfeit Vaccines and Toxicology Analysis

An example of a counterfeit drug forensic toxicology investigation appears in the literature in the realm of vaccines, where there is a growing phenomenon of fake vaccine trafficking [27]. The study for consideration took place in Brazil, between 2010 and 2020, and highlighted the problem of vaccine counterfeiting in the contexts of identifying and examining falsified influenza vaccines. Unlike the drugs mentioned previously in this review that tend to have chemically defined compositions and structures, vaccines are more chemically complex and difficult to manufacture. This study depended on laboratory analysis of suspected counterfeit vaccines that were seized by law enforcement in Brazil. The forensic toxicological investigation largely focused on identifying and quantifying pharmaceutically active ingredients in each counterfeit sample. Generally, investigators relied on analytical laboratories, where suspected counterfeit vaccines were visually inspected and their information verified. The specific toxicology tests conducted were in line with World Health Organization (WHO) guidelines and recommendations regarding what constitutes counterfeit drugs [27].

This investigation was conducted in three stages. First, there was a visual inspection of the seized vaccines, which can reveal signs of vaccine adulteration. During visual inspection, all samples were evaluated in terms of appearance, clarity, opacity, and potential presence of contamination [27]. The second investigative stage involved verification of vaccine information against the National Institute for Quality Control in Health (INCQS) database and supporting reference materials. The INCQS database was consulted as part of the laboratory management system to verify all available information against seized samples. This system records all information regarding the counterfeit drug products submitted for analysis. The third stage was the analytical tests using the seized vaccine samples. Laboratory analytical tests were performed using techniques to determine the pharmaceutically active ingredients through the single radial immunodiffusion (SRD) assay, which is considered one of the best potency assays for influenza vaccines. To complement this primary investigation process, additional analytical tests were performed, including quantification of the total protein, residual formaldehyde, and aluminum content [27].

The results from this investigation suggested strong evidence of vaccine counterfeiting. For example, the visual analysis of the seized samples revealed several irregularities in terms of printed batch number, registration number, manufacturing and expiry dates, and the layout and print color of details printed on label and outer packaging. Pharmaceutical presentation and volume of seized samples were also inconsistent, including reduced volumes and damaged vials with missing labels. The study found evidence of vaccine falsification, handmade packaging, and package inserts and labels. The analytical laboratory test outcomes corroborated suspicions that pharmacologically active substances were either absent or markedly different from the legitimate vaccines [27]. There was also commonly found to be the presence of an aluminum-based adjuvant in the counterfeit vaccines, which is not part of the composition of the genuine influenza vaccine.

There was further evidence indicating the commercialization of the counterfeit vaccines that was contrary to the country's regulatory agency protocols, indicating smuggling activity. Law enforcement investigations that took place beyond the forensic laboratory found that, in this operation, one Brazilian and three Lebanese people were involved in setting up a clandestine clinic to administer counterfeit influenza vaccines acquired in a country bordering Brazil. During the counterfeit vaccine investigation, police officials seized not only the falsified vaccines but also weapons, ammunition and silencers, and the group was charged with drug trafficking. This presence of counterfeit vaccines in Brazil was hypothesized as being due to larger structural features, including high economic benefit for criminals at the expense of weak penal sanctions (high profit and low risk); absent or ineffective national regulatory authorities; limited access to safe medical products with satisfactory quality; high prices; globalization of the pharmaceutical market; as well as the increasing complexity of supply chains [27].

Counterfeit drug analysis through forensic toxicological technologies and laboratories relates in many ways to pharmaceutical industry investigations, both of which simultaneously seek to verify the legitimacy of drugs. However, the forensic toxicology approach incorporates more diverse types of counterfeit drugs, ranging from suspected

counterfeit medicines and pharmaceuticals to illicit drugs, such as opioids and stimulants. Pharmaceutical investigations, in contrast, are more precisely targeted around medicinal-based drugs, with technoscientific procedures designed to assess their path from the point of drug evolution to patient receipt of the drug.

6.3. Pharmaceutical Investigations

Pharmaceutical companies conduct their own investigations in ways that are separate from and related to forensic crime toxicology approaches. They are similar in that both the forensic crime laboratories and pharmaceutical investigations of suspected counterfeit drugs revolve around classifying, identifying and individualizing drug samples. There are also often collaborations between pharmaceutical companies and security and law enforcement agencies [3,28]. However, forensic toxicology laboratory methods are typically more reactive to counterfeit drug findings, whereas pharmaceutical investigative strategies are more preventive. Pharmaceutical investigations and security measures tend to focus their attention more often on 'counterfeit-prone countries'. One of the key challenges for pharmaceutical companies is tracking their products during the supply chain process, as it is through this process that counterfeiters add their fake drugs to the market [29].

Typical types of investigative techniques used in pharmaceutical contexts, while not all-encompassing, include overt, covert, blockchain technology, and various AI-powered track and trace technologies. Overt and covert pharmaceutical investigations include various forms of visual and physical, as well as chemical and non-chemical approaches. Overt techniques include evaluations of the physical properties of packaging (*i.e.*, tools and dies), and the relation of these to features such as drug dosages. They aim to detect optically uneven elements regarding drug packaging, including the assessment of color-shift inks, and holograms. Color-shift inks may be embedded in drug packaging to reflect various wavelengths. The effect is observable as a change of color by changing perspectives and angles. Holograms initially appear as unrecognizable pattern of stripes and whorls, but when illuminated by coherent light, organize into three-dimensional representations. Counterfeiters can convincingly copy holograms. Covert pharmaceutical investigations may also refer to the use of ultraviolet (UV) rays to detect special UV inks on packaging. Ultraviolet inks are rendered visible when exposed to UV light instead of air.

6.3.1. Blockchain and AI Investigative Practices

Block-chain technology refers to the creation of a permanent record system in the supply chain that details drug location, contents, quality, pricing, and links to medical records, clinical trials, and healthcare data [30]. The blockchain process intervenes through the manufacturing, supply, distribution, and consumption stages of drug delivery. It records decentralized drug data as it relates to the drug, doctor, pharmacy, and medical prescription [2]. An advanced database mechanism allows for information sharing within a regulatory network. It is made up of multiple blocks, each containing several transactions. Blockchain begins with a unique identifier that is placed on the drug, which permits surveillance of the drug at various points in the supply chain, allows drug information to be communicated with regulatory agencies, and provides information regarding drug product authentication. All the blocks inside the networks are strongly linked and protected with transaction and crypto codes [2,29]. The purported advantage of the blockchain investigative strategy is to improve the identification and confirmation of counterfeit drugs. Blockchain systems enhance the potential to detect and respond to fake drugs with increased accuracy and reduce transaction costs. Although several types of blockchain exist, one example is Hyperledger, which is a fabric-based system that ensures data storage, sharing, transparency and traceability throughout the supply chain, with a focus on improving the safety of pharmaceutical items [31].

Blockchain technologies can be used in conjunction with AI and other counterfeit-reduction measures. Artificial intelligence (AI), in this context, is being increasingly utilized in the detection of counterfeit drugs due to its ability to process large amounts of data and identify patterns that may indicate fraudulent activity. AI can counter counterfeit medicines by analyzing blockchain data in real-time, enabling faster and more accurate tracking and verification of drug shipments. Blockchain can record every drug-related transaction in the supply chain, where AI works alongside blockchain to rapidly process drug data to detect anomalies, flag suspicious activities and verify product authenticity. In this context, AI algorithms can monitor drug movement from production to delivery, identifying counterfeit products or unauthorized deviations [32].

AI works in pharmaceutical investigative contexts in diverse ways, including machine learning-enabled systems, natural language processing (NLP), chatbots, and pattern recognition. First, machine learning works with blockchain systems by using drug supply chain algorithms and healthcare systems to reduce and eliminate counterfeit drugs [29]. Machine learning can identify traits and actions that are suspect or fraudulent in the records relating to counterfeit drugs,

using active data inputs to identify real-time counterfeit drug detection. Second, NLP is an AI-based image recognition and analysis mode that works at the level of text on medication labels, packaging and paperwork. This involves identifying textual variations, such as grammatical errors and discrepancies in product details, which are frequently indicative of counterfeit items [32]. It can also identify minute variations or irregularities in photos of prescription labels, packaging and even some pills that point to counterfeiting.

A third application is AI-driven chatbots, which enable greater public involvement in counterfeit drug detection by enabling consumers to report suspicious medicines. These systems can assist drug consumers in identifying counterfeit drugs based on visual cues like packaging, labelling and appearance. Once a report is made, the system can quickly forward the information to relevant authorities or manufacturers, facilitating faster responses. This enables greater consumer participation, helping to detect and remove counterfeit drugs more effectively from the market. Lastly, pattern recognition is a form of AI that works to identify patterns across sales, distribution and consumer feedback data. This can assist in identifying strange purchasing trends or sudden fluctuations in sales quantities that might indicate the introduction of fake medicines and drugs into the markets [32].

Taken together, these technologies create complementary systems. Blockchain enables transparency and data integrity, while AI adds real-time analytical capabilities, allowing for quick responses to emerging drug threats. This enables more efficient monitoring, quicker identification of counterfeit drugs, and a more secure pharmaceutical supply chain. Emerging prospects for pharmaceutical investigative approaches include the advent of nanotechnology to support anti-counterfeit drug techniques. Blockchain, AI, and nanotechnology are advocated for improving counterfeit drugs' traceability, genuineness, accuracy, efficiency, and detection abilities within the supply chain. The pharmaceutical industry's implementation of these innovations at national and global levels is intended to empower consumers, reduce counterfeit drugs in licit and illicit markets, protect public health, and improve healthcare system quality [32].

6.3.2. Challenges with Blockchain Technologies in Sri Lanka

The previous discussion in this section outlines the promises of emerging pharmaceutical investigative strategies. However, adopting new pharmaceutical investigative technologies is quite inadequate in most developing nations due to a lack of infrastructure, social hurdles, and economic and financial constraints [31]. These challenges, as they relate to the drug chain, have led to life-threatening issues that result in thousands of deaths in developing countries. The example outlined here refers to some of the challenges in adopting blockchain technology in the Sri Lankan pharmaceutical supply. In Sri Lanka, counterfeit drugs are a public health concern. Pharmaceutical supply networks in this region are insecure and vulnerable to fraudulent activity. For example, foreign firms provide more than 80% of the country's pharmaceutical needs, with the remaining 20% produced domestically [31].

Blockchain technologies have been implemented to a degree in Sri Lanka, and this technology is viewed as one of the best options for analyzing, monitoring, and ensuring the production processes of possible pharmaceuticals. At the same time, packaging and pharmaceuticals in this region are becoming increasingly susceptible to counterfeit attempts and practices, making it hard for consumers and law enforcement to adequately detect fake drugs without formal forensic toxicological chemical analysis [31]. Consequently, factors preventing blockchain's adaptability in Sri Lanka include compatibility issues, relative advantage, human resources (*i.e.*, lack of upper management support), complexity, cost, and technology infrastructure and architecture in the pharmaceutical supply chain. As a developing country, the Sri Lankan pharmaceutical industry lacks the requisite capacities to successfully implement blockchain technologies in a way that adequately improves the transparency and traceability of the pharmaceutical supply chain. This leaves the Sri Lankan pharmaceutical industry particularly vulnerable in acquiring the advanced blockchain technologies and laboratory equipment necessary for investigating the quality of pharmaceutical products and tracing the internal supply chain.

6.4. Coordinated Response Investigations

The final counterfeit drug investigation is coordinated responses. A global debate has emerged about the appropriate means to address the illicit trade in counterfeit drugs. The dominant security perspective is to mobilize investigative tactics through a multitude of regulatory resources to combat this form of transnational counterfeit drug crime. There is consensus that the global trafficking of counterfeit drugs is difficult to quantify, largely because of the adaptable criminal element of this drug trade and lack of adequate surveillance. Recent investigations and law enforcement efforts have uncovered large-scale illegal counterfeit drug manufacturing in multiple current and emerging markets, links to organized crime and terrorism, and have, to date, instituted global drug seizures in both producing and

consuming countries [33]. As such, preventing and disrupting counterfeit drug crime and corruption depends on key national and international regulators' recognition, coordination and active engagement.

6.4.1. Global Coordination

Institutions that are starting to collaborate to reduce the counterfeit drug phenomenon at the international level include the World Health Organization (WHO), the World Customs Organization (WCO), the United Nations (UN), and Interpol, and related patient safety groups, law enforcement, civil society, and the private sector. To date, International responses have successfully reduced counterfeit drug crime and corruption. However, critics of such approaches argue that the existing and emerging initiatives lack policy coherence and there are limits to their ability to coalesce and cooperate around a unified purpose [33]. The United Nations Office on Drugs and Crime (UNODC), for example, specializes in establishing policy and coordinating actions in combating and preventing many forms of transnational organized crime, including corruption, terrorism, and the trade and trafficking of many types of counterfeit and illicit drugs worldwide. UNODC has partnered with Interpol, WCO, and public and private sectors to lead initiatives that directly target counterfeit drugs through multi-sectoral law enforcement and border control programs. The UN Commission on Crime Prevention and Criminal Justice (CCPCJ) has simultaneously supported and empowered the UNODC to govern the counterfeit drug trade by conducting research, providing technical assistance to member states, and facilitating cooperation with other international organizations. In this way, the UNODC represents one of the most successful international bodies in engaging and coordinating the multitude of fragmented agencies and institutions currently addressing counterfeit drugs. Enhanced global health governance through coordinated responsibilities of multiple institutions is a coordinated investigative approach to prevent and reduce transnational counterfeit drug crime and enhance public health outcomes [33].

6.4.2. The American Coordinated Response

There are also coordinated responses at the national level. For example, the United States (US) has invoked coordinated response teams (CRTs) that respond to counterfeit drugs through an amalgamation of postmortem toxicology, drug toxicology, and pharmaceutical investigative strategies. A CRT typically consists of forensic toxicology laboratory members, medical examiners and coroners, local hospital personnel, local and state poison control systems, law enforcement, social services and outreach agencies, and media outlets. This collaborative investigative strategy is centered on collecting and analyzing medical and case histories of drug-affected individuals and collecting relevant biological samples and physical evidence. From a forensic toxicology standpoint, drugs and other samples are quickly processed to avoid delays or improper storage, handling, or analysis that could result in higher numbers of overdose cases and/or deaths. Further measures include sending out red alerts and public health warnings about illicit and counterfeit drugs through multiple communication avenues such as radio, television, and social media. This notifies the public about the identified existence, prevalence, and potential harms associated with counterfeit and other illicit drugs. Health and social workers, police, and outreach volunteers are in place to talk to people on the streets about these issues. Police and toxicology laboratory personnel can work to identify the online sites and/or online pharmacies selling illicit and counterfeit drugs and remove the websites so that the drugs are unavailable for public consumption. These collaborative efforts aim to reduce counterfeit drug-related harm, overdoses, and deaths [19]. They also assist in the production of evidence for the subsequent prosecution and adjudication of corrupt and criminal drug networks. Global and national coordinated counterfeit drug investigations operate in conjunction with forensic medicine, forensic toxicology, and pharmaceutical investigative strategies. These investigation types have been discussed separately for the purpose of this discussion, although there are many overlaps between them. Many challenges emanate from all investigation styles that occur at these multiple levels, including technoscientific, geographical, the production of valid evidence, and enforcement strategies.

7. Challenges to Counterfeit Drug Investigations

While not an exhaustive list, counterfeit drug investigators face notable and multiple challenges. These challenges range from international and national issues (*i.e.*, politics, security, legislation and enforcement); public health and safety matters; the supply of counterfeit drugs in both virtual and material environments; forensic toxicological and law enforcement investigative techniques and approaches, including the chemical composition of drugs; and at the level of pharmaceutical innovation. International and national challenges pertaining to the counterfeit drug phenomenon include the fact that the counterfeit drug trade damages economic growth, and undermines legitimate governance and trust in

political stability and the rule of law. There are legislative challenges in detecting and prosecuting those responsible for counterfeit drug-related crimes. This is particularly apparent in countries that do not possess relevant legislation to target these drug offenses. The countries that may have relevant drug legislation in place often have weak penalties, which encourages counterfeit drug operators to take risks as the financial rewards may outweigh the penalties [3]. There is also an uneven distribution regarding counterfeit drug testing between higher- income and middle- and lower- income countries. It is harder to do forensic toxicological investigations for counterfeit drugs in middle- and lower-income countries due to the cost of establishing sophisticated forensic systems and because the forensic expertise in these countries may not be at the same level as higher-income countries. This creates a vulnerability in forensic toxicological technologies and infrastructure that is skewed depending on global geographical location. The lack of adequate forensic toxicological apparatuses in middle- and lower- income countries increases the chance that counterfeit drugs will continue to evolve and disproportionately impact the health and safety of consumers (*i.e.*, lack of proper medical treatment, overdoses and deaths) [3].

The manufacture and supply of counterfeit drugs also bring significant challenges to counterfeit drug investigators. Counterfeit drugs are easily available due to the growth in the use of postal services to deliver these products, leaving the source of the drugs difficult to discern [3]. For law enforcement and drug regulators, determining the origin of counterfeit drugs is difficult as it is often only post-shipment that drugs may be detected and seized. This relates to the fact that many counterfeit drugs originate from rogue on-line pharmacies, the dark web and dark markets, where locating, measuring and seizing counterfeit drugs can be difficult as they move unpredictably through this virtual supply chain [15]. This leaves considerable uncertainty regarding the origin of counterfeit drugs, particularly as they are linked to rogue and dark markets, and a large portion of these drugs are undetected and undeclared. A further challenge is that counterfeit drugs are difficult to detect since they are distributed in small volumes, yet produced in large doses, making them easy to conceal and transport. Detecting and seizing such drugs is then quite difficult [9]. To date, there have been some successful disruptions and eradication of dark counterfeit drug markets by law enforcement, however, these markets tend to re-emerge in new forms [15]. The distribution of counterfeit drugs is compounded by the fact that consumer demand for both counterfeit and other illicit drugs is quite high and there is a willingness by consumers to buy drugs virtually without concern that the drugs may not be properly formulated.

The forensic and pharmaceutical toxicological investigative context is another area that presents further challenges. These include issues with postmortem drug changes, the sensitivity and variation in scientific technologies, a lack of necessary information about counterfeit drugs, and the ability of counterfeit drug operators to change the chemical composition of drugs to evade detection. Regarding forensic toxicological postmortem investigations, detecting counterfeit drugs may be difficult due to 'postmortem changes'. These postmortem concentration changes can lead to counterfeit drug identification problems [9,21]. This occurs when drug concentration transitions into the form of metabolites in the human body, and the metabolites change in form from the living to death conversion. There is further instability in measuring metabolites as they relate to drug compounds, including potential limited knowledge of counterfeit drug metabolism on the part of the medical investigator. Regarding existing and emerging fentanyl analogues, for example, there are limited and unclear relations established between the metabolite process as it relates to drug intoxications and fatalities. The fentanyl metabolism data is therefore limited at the point of determining the specific molecules in biological samples that indicate fentanyl consumption [9]. The issue of limited counterfeit drug data is also a global issue, including limits in compiling a comprehensive and updated list of counterfeit drugs and their analogues, properties and drug metabolites. The consequence is that many acute and fatal intoxications by counterfeit drugs are under-reported or under-estimated because of the medical difficulties in identifying new drug compounds frequently appearing in the drug trade. Challenges in investigating counterfeit drugs are further compounded by the fact that new derivatives of falsified and illicit drugs are continually being produced to circumvent the laws that ban their abuse. Once a drug is categorized as prohibited, new versions and derivatives are synthesized and introduced into the drug markets [9].

Another forensic toxicological challenge is the potential lack of sensitivity inherent to scientific techniques as they are necessary to detect many of the counterfeit drug-related chemicals and metabolites. From a medical toxicological perspective, detecting and identifying counterfeit drugs is often difficult both in hospital settings and in postmortem forensic analysis because regular testing of these drugs is infrequently performed [9]. Forensic toxicological procedures may also produce variable results, which leads to a lack of consistency depending on the technology used. Moreover, in the case that there are no vials or packages containing the suspected counterfeit pills or tablets at the sample site/crime scene, the medical toxicological analysts will have no material or substance to compare to the ingested drug. From a drug toxicological perspective, counterfeit drug operators can make falsified and counterfeit drugs that incorporate crude active ingredients, which are chemicals that have not undergone the appropriate purification steps required to

meet pharmaceutical standards. Forensic toxicology investigators may have difficulties identifying these crude ingredients as they render more sophisticated and subtle counterfeit drugs. The counterfeit drugs made from such crude chemicals would pass most forensic toxicological tests. Only highly sophisticated forensic toxicology analysis, which is often very expensive to perform, could adequately discern this crude material from purified trace ingredients.

Forensic toxicological drug investigations can typically identify a drug with no active ingredient or one made under manufacturing negligence, but the more sophisticated counterfeit drugs often resist easy detection. In the case of forensic uncertainty regarding the status of a counterfeit drug, the focus can shift to the drug's appearance. This includes analyzing the tablet materials, including coatings, although coatings can also interfere with the correct chemical analysis of drug content, leading to confused or inconclusive results. In this context, AI-induced forensic medicine and toxicology also have ethical limitations. AI is useful in promoting efficiency and accuracy in drug detection and patterns, however, critics argue that AI will impede the traditional practice of human judgment. Relatedly, it is debatable whether the opinions and data provided by AI in forensic medicine will be trusted by investigating personnel in law enforcement and pharmaceutical industries, the judiciary level, and the public [22]. The AI issue is further compounded by the fact that investigatory agencies (*i.e.*, law enforcement and border officials), regulatory bodies (*i.e.*, drug regulators) and pharmaceutical companies are wary of divulging and publicizing all their investigative techniques as this would provide counterfeiters with more resources [8]. The inherent focus and dependence upon scientific and technological procedures to detect, categorize, assess and produce counterfeit drug-related evidence is all-encompassing in contemporary investigative strategies. Contrary to this reliance on technoscientific processes, the remaining points outline the significance of human and cognitive-based abductive logic as central to counterfeit drug investigations. Counterfeit drug information may produce unique, novel, and 'surprising' types of evidence that needs to be interpreted in a flexible way due to the ongoing manipulation of the chemistry and biology of these drugs at both the bodily level and the composition of the drug itself.

8. The Logic of Abduction as an Investigative Mode

The logic of abduction is useful to counterfeit drug investigations as it is open-ended enough to address dynamic, interconnected and uncertain evidence that is often produced from forensic and medical investigations. An open-ended investigative logic seems necessary to encompass the numerous counterfeit drugs, online environments, operators and operations, and investigative strategies deployed. As such, the logic of abduction is presented as a form of reasoning that allows for the introduction of new ideas and hypotheses. Abduction was formulated predominantly by philosopher Charles Peirce (2014) in conjunction with the related logics of deduction and induction. In his work entitled 'Illustrations on the Logic of Science', he outlines these three logical paradigms [34]. Deduction is the process of formulating an absolute conclusion based on generally accepted statements of facts. This involves reasoning about the consistency or concurrence of a recurring pattern. Induction relates to applying evidence to draw logically possible conclusions, but it is not necessarily completely accurate. This is the process of forming a generalization based on what is observed, where the conclusion is quite likely, but not certain, and involves reaching a tentative conclusion. Abduction is a form of reasoning that explains a logical operation and introduces a new idea. Abduction starts with observations and conclusions achieved from inductive and deductive processes and suggests the simplest and most likely outcome from them [35]. In this sense, abduction is these three modes' most creative and spontaneous reasoning.

A more specific consideration of Peirce's (2014) abduction reveals the element of discovery, which is the stage of inquiry where theories and hypotheses are generated. Here, it is a form of generative reasoning that begins with observing scientific information, including anomalies, to explain novel or unexpected phenomena. Abductive reasoning begins with an incomplete set of observations, from which these observations proceed to the likeliest possible explanation. It is a process of inquiry that cycles between generating 'doubt' and generating 'belief'. Abduction encompasses the possibility of anomalous theoretical and empirical cases through a form of inference based on the meanings of signs or evidence [36,37]. In all, abduction uniquely juxtaposes practice (singular, unique), theoretical dimensions (rules, generalizations, universals), imagination, and creativity.

In addition to Peirce's (2014) conception of abduction, related philosophies complement his viewpoint. Linus Pauling (1960), author of the Pauling Principle, states that, 'the process of getting good ideas is to get lots of ideas and throw the bad ones away' [38]. For Pauling, there must be a willingness to generate both good and bad ideas, and for the process of discovery to occur, there must also be false starts, failures, and disappointments along the way. Relatedly, Karl Popper (2002), author of 'The Logic of Scientific Discovery', argues that discovery has 'no logic'. Popper's proposition assumes that science should adopt a methodology of falsifiability, which means that no number of

experiments can ever prove a theory, but a reproducible experiment or observation can refute one. A hypothesis becomes more probable the more it is tested without falsification [39].

An extension of the abductive logic that resonates with the online aspects of the counterfeit drug supply is the notion of digital abduction. Digital abduction uses the principles of abduction to assess, investigate and approach counterfeit drugs from digital and virtual perspectives. Digital abduction is situated in the larger 'forensic social sciences', which is an emerging discipline that uses abductive reasoning as a source of preliminary predictions in large digital data sources [40]. Digital abduction is a derivative of abductive reasoning in virtual and/or online environments. It situates abductive logic as inseparable from 'digital footprints', such as big data and computational tools, that put forth information online about counterfeit drug-related supply and consuming behaviors. Big data describes large, hard-to-manage volumes of structured and unstructured data, which inundates organizations and society in an ongoing manner. Digital abduction is concerned with the trail of data an individual leaves behind when using virtual or online platforms (*i.e.*, online pharmacies, emails, social media, and other online data). In virtual contexts, abduction refers to the potential for tracking and investigating an individual's online activities and devices. Digital abduction allows for carefully compiling evidence from digital traces to generate new hypotheses and theories. The extension of digital abduction from abduction more generally can lead to the potential for theoretical diversity in the context of this logic [40].

The Peircean abductive logic and related philosophies relate to forensic investigations in epistemological ways (how to know), ontological ways (what to know), and normative factors (how to value the process of solving crimes) [35]. The abductive forensic investigation involves 'finding and following clues' and eliciting new knowledge [41]. Abduction, then, does not necessarily produce clear answers, but rather depends on a process of trial and error [42]. Abduction, in the context of counterfeit drug investigations, involves a creative process of producing new hypotheses and theories, which incorporates 'surprising' forensic data and evidence and produces tentative conclusions [40]. This is not necessarily entirely novel, as the intellectual tasks performed by forensic and medical investigators already involve abductive reasoning [35]. However, abductive-based investigations move beyond a sole reliance on denotive, technical and analytical assessments and evidence, especially considering the breadth of forensic science and technology available in many crime investigation apparatuses.

Forensic semiotics can be thought of as a specific, related dimension of the forensic abductive investigative process, particularly in relation to evidence. Semiotics is a complex series of philosophies and practices that deals with studying and interpreting signs and symbols. Suppose forensic evidence, including counterfeit drug information, is conceived of as a series of signs and symbols to be interpreted by investigators. In that case, this prioritizes the interpretation of evidence through the processes of inferential or 'informed guessing' [35]. The signs and symbols inherent to forensic evidence may assist investigators in producing logically derived assumptions, conclusions, and 'new truths', which can then be modified or rejected. Forensic semiotics, here, are visual, scientific and analytical tools that allow for the merging of disciplinary boundaries, while maintaining an acceptable level of scientific rigor [43]. Forensic semiotics, as related to the logic of abduction, are both conceptual and practical as they lend to a mode of informed guessing about the ways in which multiple evidence are connected to one another (*i.e.*, the chemical composition of counterfeit drugs in the virtual contexts that they may be distributed). Each piece of forensic evidence has a multiplicity of possible meanings, which can be translated into a theory of crime commission and an offender profile [35]. Here, forensic-based abduction, digital abduction and semiotics refer to the inherent cognitive and human processes of reasoning about counterfeit drug evidence in open-minded, creative and flexible ways to encompass the complexities inherent to these drugs. The next section looks at a few possibilities for applying forensic abductive and semiotic logics to counterfeit case scenarios.

9. Abduction in Counterfeit Drug 'Investigative Futures'

Abduction and digital abduction are logical practices that can be applied to counterfeit drug investigative strategies in their current operations, but also in line with emerging investigative challenges. Abductive logic seeks to introduce new ideas through creative, logical processes, find evidence, and elicit new knowledge. Abduction relates to forensic investigations along epistemological, ontological and normative lines to determine and value knowledge. Digital abduction is an extension of abductive reasoning that highlights the ways to assess, investigate and approach counterfeit drugs from digital and virtual perspectives. It is a derivative of abductive reasoning that focuses on big data and computational tools. As such, certain key challenges inherent to contemporary counterfeit drug investigations may benefit from prioritizing abductive-based approaches in contrast to solely scientific and technological assessments alone.

First, the types of forensic toxicological evidence derived from counterfeit drug investigations could gain from abductive reasoning generally, and forensic semiotics specifically. In counterfeit drug-related autopsies, for example,

biological samples are often analyzed in terms of drug metabolites, which are a type of evidential biomarker. During the forensic postmortem toxicological analysis, there are currently limits relating to the implementation, development, validation, and improvements of forensic techno-scientific methods to detect counterfeit drug ingestion at the level of metabolite analysis and classification level. This includes the potential lack of sensitivity inherent to scientific techniques as they are necessary to detect many counterfeit drug-related chemicals and metabolites, which may lead to variable results depending on the technology used. These techno-scientific challenges are further compounded by the fact that new derivatives of falsified and illicit drugs are continually being produced to circumvent the laws that ban their abuse.

Artificial intelligence (AI) has been introduced to combat some of these challenges, particularly in post-mortem interval (PMI) estimation, personal identification, and tissue/fluid identification. AI is also used in forensic medicine to open new perspectives by analyzing big data and creating new prediction models to assist forensic experts in forming more accurate, rapid and uniform opinions related to forensic case examination. This occurs by comparing the data from investigator findings with the data available from machines [22]. AI algorithms are used to analyze samples more accurately and efficiently and are combined with robotics to automate some aspects of toxicology testing, such as collecting and transporting samples, understanding the functioning of biomarkers and molecules, identifying new psychoactive substances, and prevent the development of emerging counterfeit drugs. These algorithms seek to create expert systems that make predictions or classifications based on input data, connect various databases and other sources of information in the investigative process, and link data to current and past crimes [22].

However, there are limits to AI in forensic medicine where human-based abductive reasoning can fill these spaces. AI limitations include costs, the paucity of data available, and the legal value of the data analyzed and reported by AI. Importantly, the human investigator's role is still essential, particularly in the capacity to assess scientifically generated data analyzed per specific case abductively. Investigator-derived abductive reasoning is a more influential and creative logic to understand toxicological data about counterfeit drug trends, interpret drug surveillance, and identify and hypotheses about emerging counterfeit drug-related dangers as they pertain to overdose and death determinations. In the evidentiary realm, forensic semiotics are also necessary to discern, decipher, and create conclusions relating to metabolites and other tissue and fluid markers, as well as data and profiles related to counterfeit drug ingestion.

Second, digital abduction is particularly relevant to pharmaceutical investigations' blockchain and related AI features, as they encompass virtual environments, big data and computational tools. Again, block-chain technology refers to creating a permanent record system in the supply chain that details drug location, contents, quality, pricing, and links to medical records, clinical trials, and healthcare data [30]. Blockchain can record every drug-related transaction in the supply chain. AI works alongside blockchain to rapidly process drug data to detect anomalies, flag suspicious activities and verify product authenticity. AI algorithms can monitor drug movement from production to delivery in this context, identifying counterfeit products or unauthorized deviations. Blockchain technologies can be used to prevent counterfeiting efforts, where AI works to process large amounts of data, identify patterns that may indicate fraudulent activity, and analyze blockchain data in real-time [32]. The blockchain and AI synthesis can also interpret, investigate and act against counterfeit drug operators and operations that are produced through pharmaceutical investigations. Blockchain and AI are, in this sense, complementary to the investigatory process and not entirely sufficient on their own to decide what data is most valuable and what actions are most relevant to prevent and disrupt counterfeit drug operations.

Abduction and digital abduction coalesce in the third challenge for investigative futures, which relates to educating the public about the high overdose risks presented by counterfeit and falsified drugs, particularly as this may prevent further risks of purchasing suspect drugs online. Recommendations to date tend to highlight increasing outreach and linkage care among those who use counterfeit prescription pills (*i.e.*, pills obtained without legitimate prescriptions), improving access to harm reduction tools, such as fentanyl test strips to reduce unintentional exposure, and increasing naloxone supplies to reduce opioid overdose. Additional areas for abductive reasoning are in creating new practices around counterfeit drug surveillance in hospitals that enhance laboratory testing of biological material from patients with signs and symptoms of a counterfeit drug overdose and creating further identification practices for drugs and drug paraphernalia [20]. Finally, regarding the illicit counterfeit drug market, more imaginative solutions could be directed towards creating and sustaining services to sanctioned drug-checking services, and overdose prevention sites, and working to reduce the stigma associated with drug use [25]. The application of abductive modes of reasoning to counterfeit drug investigative practices in the above-mentioned outline is only a beginning, as it indicates the importance of human logic in these circumstances.

10. Conclusions

The presence and continuing emergence of the counterfeit drug phenomenon exist on a global scale, through both material (*i.e.*, the streets, hospitals) and virtual sites (*i.e.*, online pharmacies, the surface and dark webs), and by multiple counterfeit drug operators and operations. Investigating counterfeit drugs across these lines is challenging. The counterfeit drug phenomenon is particularly unique in that it is continuing to emerge, expand, update and diversify at international levels and across multiple domains. The production and distribution of counterfeit drugs are adaptable, innovative, and dynamic, which may create uncertainty for investigators. Investigative strategies continually require new conceptual modes (hypothesis, discovery, logic, theorizing) and practices (digital and material, technological and scientific practices) to offset counterfeit drug trends. The manufacture of counterfeit drugs is ever-changing (*i.e.*, drug analogues and derivatives), which results in the need for investigative techniques that are equally advanced and collaborative across multiple domains (*i.e.*, law enforcement, health, medical and pharmaceutical industries, material/internet/digital/virtual, bodily/corporeal, scientific and technological). Consequently, disciplinary boundaries are increasingly conjoined in toxicological and related counterfeit drug knowledge and practices.

The logic of abduction and digital abduction are presented as modes of investigative reasoning that are creative and open-ended enough to deal with continual efforts by offenders to evade detection in the manufacture and distribution of counterfeit drugs. Abduction, and the related digital abduction and forensic semiotics, are logical processes that contain generative reasoning to observe, identify and classify counterfeit drugs in material and virtual domains. This form of abductive reasoning can generally be applied to the forensic toxicological investigations of drug anomalies in the chemical composition of the drug, the individual who has consumed the drugs, and the packaging, manufacturing or supply chain processes. Toxicology results are often novel, unexpected, inconclusive and 'surprising' as each health matter, overdose or postmortem case is unique. The specific logic of digital abduction allows for forensic investigations to operate at virtual levels to structure data into meaningful knowledge categories and open the possibilities for critical interrogation. This is due to digital counterfeit drug data emerging in virtual pharmacies surface and dark web environments.

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