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# **Pharmacovigilance: There is a Need for All to Get Involved!**

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*The sole author designed and prepared the manuscript.*

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## **ABSTRACT**

The harm(s) a drug may cause may not be known at the time it gains market authorisation. Drug regulatory agencies weigh the benefits that the drug presents against the potential harms it could pose and allow it to be marketed if it is believed that the drug has a favourable risk-benefit ratio. Regulatory agencies then evaluate the drug's risk profile as it is used on a large scale and institute remedial measures if found necessary. Data is needed in establishing that an Adverse Event (AE) accompanying drug use is, in fact, an Adverse Drug Reaction (ADR), and in carrying out the functions outlined above. This paper explores some of the issues involved, the importance of data in the work of regulatory agencies and draws attention to the need for all to facilitate the work of regulatory agencies.

**Keywords:** *Adverse Event (AE); Adverse Drug Reaction (ADRs); Sponsors; Spontaneous Reporting System (SRS); pharmacovigilance; Ghana.*

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## 1. INTRODUCTION

While the primary focus in the development of a drug is finding a treatment for an illness, the safety of users is paramount as drugs are essentially chemicals [1]; the prospect of them causing harm is ever present especially if not well formulated or predisposing circumstances are presented. Thus beyond the obligation to guarantee that the intended product is well formulated, drug producing entities (sponsors) have a moral duty to ensure that adequate information has been provided to the intended users. Consumers are also responsible for safety in the use of drugs as sponsors and drug regulatory bodies [2]. The need for a consumer to follow to the letter any instructions pertaining to the use of a medication can hardly be overemphasised. Checking the expiry date and the integrity of the packaging of a medication, for instance, are some of the common sense practices all must foster.

The primary onus to safeguard public health, as far as the use of medicines is concerned, lies with regulatory bodies who are expected to be strident in ensuring that only medicines that have passed the required safety scrutiny obtain marketing license or cause the removal from the market medicines that have assumed questionable safety credentials. Drug development is a costly enterprise and drug development entities, being commercial, are expected to recover their investment and satisfy the expectations of their shareholders [2]. Without the superintending role of regulatory bodies, a less conscientious sponsor could be baited into marketing unsafe products [1] by the huge market for drugs because diseases are thriving regardless of the strides the profession of medicine has made [2].

## 2. ADMINISTRATION OF DRUGS AND RELATED ISSUES

### 2.1 Adverse Drug Reactions

An adverse drug reaction, commonly referred to as side-effect, is any harmful effect of a drug [3,4]. The dynamics influencing the nature and severity of an ADR comprise age, gender, genetic make-up, weight, dose regimen, disease condition, the overall health status of the individual using the drug and chemical composition of the drug [3,4]. The discourse on ADRs is typically about the harm(s) a drug can cause at the prescribed dose level as almost

invariably most drugs will cause harm if not used as the dose regimen requires [2].

#### 2.1.1 Types of ADRs and their characteristics

The way an ADR is regarded depends on the manner it is caused, how it manifests itself and its severity [2]. In their article "Adverse Drug Reactions: Definitions, Diagnosis, and Management", Edwards and Aronson [5] presented six ADR classes, namely: "A: dose-related (Augmented), B: non-dose-related (Bizarre), C: dose-related and time-related (Chronic), D: time-related (Delayed), E: withdrawal (End of use), and F: failure of therapy (Failure)" [5], taking a cue from the works of other authors [6,7,8,9]. Adverse drug reactions that are often discussed are the A and B types. As indicated above, drug reactions that result from understandable chemical processes and are related to dose are said to be Type A reactions (pharmacological reactions) and those reactions that cannot be anticipated from the chemical composition of the drug and are not dose dependent are referred to as Type B reactions (idiosyncratic reactions). These reactions result from obscure chemical processes and persons affected by them are allergic to or their genetic composition predispose them to a hostile immune response to the medication [1,4,6,7,8,10].

Some adverse reactions are mild, easy to manage and relatively common than others. "Weakness, sweating, nausea and palpitations" are in this class of reactions [4]. As alluded to in the foregoing, some adverse reactions are uncommon; they tend to be more serious and find expression in a minority of people [1,4]. Reactions in this category are "skin rashes, jaundice, anaemia, a decrease in the white cells count, kidney damage, and nerve injury that may impair vision or hearing" [4].

#### 2.1.2 Prevalence of ADRs

Type A reactions are in the majority, constituting over 80 % of all side-effects [10,11]. In the United States of America (US), around 3 to 7 % of hospital admissions are due to the side-effects. About 10 to 20 % of patients admitted to hospital for causes other than ADRs experience side-effect(s) during their stay, of which severe reactions account for about 10 to 20 % [5]; for the United Kingdom (UK), the respective values are 5 % and 10 to 20 % with 0.1 % of the side-effects resulting in deaths [12]. Results from

studies involving three hospitals in the UK, which are consistent with the above results, put the proportion of hospital admissions that is due to side-effect at 5.2%. The proportion of patients admitted for causes other than ADRs that experience side-effects during hospital stay was estimated at 14.7% and the proportion of side effects that resulted in death was found to be around 0.15% [13,14]. An international study published in 2014, indicated that on the whole, the ADR prevalence rate for England, Germany and US are 3.22%, 4.78% and 5.64% respectively [15]. For countries with low literacy rates, amorphous ADR reporting schemes or tenuous regulatory structures the ADR prevalence are probably higher [2].

Table 1 presents a classification of ADRs based on prevalence, as provided in the British National Formulary [16].

**Table 1. Prevalence classification for ADRs**

Prevalence	Description
Greater than 1 in 10	Very Common
1 in 100 to 1 in 10	Common
1 in 1000 to 1 in 100	Uncommon
1 in 10 000 to 1 in 1000	Rare
Less than 1 in 10 000	Very Rare

Source: British National Formulary, September 2017 – March 2018 [16]

### 2.1.3 Identifying ADRs

On average, less than 3000 subjects may have been exposed to a medication through clinical trials by the time it is marketed [1]. This number is substantially smaller than the number of patients that use the medication when it has gained marketing approval. As a result, adverse drug reactions that are rare in occurrence are often not detected at the development stage, where the number of subjects on whom a medication is trialled is, for various reasons, small [1,12,17]; the trial sample size may be enough to detect side-effects with prevalence of 1 in 1000 to 1 in 10, but may not be adequate to profile them in their entirety [12]. Thus detecting ADRs with incidence of 1 in 10000 or less in clinical trials is much slimmer [16,18]. This situation is compounded by the fact that some side-effects occur as a result of drug-disease (besides the one under treatment) interaction or drug-drug interaction [4,12] which are usually not the primary motivation for clinical trials. It is therefore not uncommon to detect problems with a drug after it has gained marketing approval, as,

among other things, the post-approval pool of subjects who use a drug is both more diverse and bigger than that of clinical trials [17,18,19].

The limited time within which clinical trials are conducted, given contending factors, may preclude the detection of ADRs that results from continuous use of the drug over an extended period or ADRs that manifest with time (long-latency) [17,19].

Factors that may lead to the non-detection of ADRs at the trial stage could include the situation of the primary responsibility for conducting safety test resting with sponsors and not regulatory bodies [1,20,21]. Thus a failure on the part of a sponsor to do due diligence on all precautionary measures regarding the safety of a medication may result in an ADR eluding detection before marketing approval has been granted. Additionally, what might finally present as a result of the use of a medication may be beyond man's recognition, as nature is not totally explicable [1].

## 2.2 Pharmacovigilance

Given the factors that make it impossible to detect all ADRs before marketing approval, drug regulatory bodies such as the Food and Drugs Authority of Ghana (FDA, Ghana), Medicine and Healthcare Products Regulatory Agency (MHRA) and Commission on Human Medicines (CHM) of the UK and the Food and Drugs Administration of the US (FDA, US) are left with no alternative than to decide whether a prospective medication present an acceptable balance between the benefits and the potential harms associated with it on the basis of the medication's development dossier submitted by the sponsor, and if so grant the drug interim marketing approval [20,21] whilst keeping tabs on the adverse events attributed to the drug as it is used by the general populace. The data gathered through this means allow drug regulatory bodies to fully understand the attributes of the medication. They are then in a position to take corrective action where necessary, which could include dose revision, withdrawal of product and provision of advice on what is appropriate to the public and healthcare practitioners, among others [22,23]. The World Health Organization's WHO Collaborating Centre for International Drug Monitoring (Uppsala Monitoring Centre), in Uppsala, Sweden, provides a forum for, inter alia, cooperation in drug monitoring by member countries of WHO through their drug regulatory agencies [24].

Ghana became a member of WHO's International Monitoring system in November 2001. It was the 65<sup>th</sup> and the first country in West Africa to join the programme [25].

Administering drug use as described above may well be problematic ethically as users may be unintentionally exposed to harm if a drug has an unknown adverse effect, but regulators can scarcely do anything else because the development of a drug is an intricate enterprise that comes with negotiating a delicate tradeoff between several competing factors which 'militate against' the process. The issue of ethics which requires the educated consent of human subjects of clinical trials, could also lead to lack of volunteers [2].

Tracking the use of drugs and the associated adverse events to discover hitherto unknown harms related to them or changes in their adverse reaction profiles or their misuse or abuse, while these drugs are available for use by the public, so that regulatory measures can be effected if warranted, is known as Pharmacovigilance [17,19,23]. The range of activities undertaken in pharmacovigilance comprise identifying previously unknown ADRs (single drug reactions and those that are the consequence of drug-drug interactions), by keeping surveillance on drugs that are on the market, especially those whose indications (context of use or diseases) have been augmented and recently approved ones [17,19]; studying the interrelationship between drugs belonging to same therapeutic class; finding the effect genetic makeup, drug class, "dose, age, gender, underlying disease" [19] and other relevant variables have on certain subpopulations of users; safeguarding the correct use of over-the-counter drugs (OTCs) (including off-label use) and prescriptions-only-medicines (POMs) by health professionals and the general public [17,19], and "providing information to healthcare professionals and patients to optimise safe and efficient use of medicines" [23]. While the focus of pharmacovigilance was initially on untoward effects of drugs, its scope has now broadened to include surveillance for counterfeited or sub-standard medicinal products, with the coming on of what appears to be havens for the production and 'black-markets' for the sale of such products, as these products compromise health delivery and are responsible for loss of life and economic damage.

Regulatory bodies can, with the collaboration of sponsors, take one or more of several remedial measures contingent on the urgency and gravity of the situation requiring regulatory action. This include modification of labels, augmenting warning and precautionary messages on information leaflets and packages; dose modification, limiting indication, mandatory monitoring of patients; seeking informed consent of patients, restricting prescription and distribution of product; suspension of marketing and distribution, banning of product, withdrawal from market, and revoking licenses [17,23,26,27].

It is worthy of note that other considerations (commercial and not for safety or efficacy reasons, for instance) could cause the withdrawal of a medication from the market by the Market Authorization Holder (MAH), as in the case of the withdrawal of Augmentin Infant Drops and Nospa Forte Tablets (80mg) from the Ghanaian market by Glaxo-SmithKline and Sanofi Aventis respectively [28].

## 2.3 Spontaneous Reporting System

Drug regulatory bodies and sponsors have several sentinel schemes that facilitate drug safety surveillance. One of these schemes, commonly known as the Spontaneous Reporting System (SRS), encourages the reporting of AEs accompanying drug use directly to regulatory bodies or indirectly through sponsors, who are obliged by regulation to forward the information to the regulatory bodies [17,29,30]. It is known as the FDA Adverse Event Reporting System (FAERS/ MedWatch) in the US and the Yellow Card Scheme in the UK (probably due to the Yellow forms used to report adverse events) [30,31]. Ghana's spontaneous reporting system, implemented through the 'Blue Form', received a total of 1607 Individual Case Safety Reports (ICSRs) in 2016 [28].

### 2.3.1 Difficulties with the spontaneous reporting system

The spontaneous reporting system has been key in identifying uncommon harms associated with drugs, particularly newly approved ones [26,32]. An instance of such facilitation is the discovery of the link between remoxipride and aplastic anaemia [12]. Notwithstanding this frontline role, it is identified with several problems:

Adverse events associated with drugs use are not reported as often as they occur [19,33], and the degree of under-reporting is more pronounced in the case of some adverse events and drugs than in others. In Spain, Alvarez-Requejo et al. [33] found that non-serious events are not reported to the same extent as serious events. Newly marketed medications and unclassified events tended to have relatively higher reportage. They also found that gastrointestinal and psychiatric disorders were comparatively more under-reported, and anti-infectives and cardiovascular medications are predisposed to being cited as the cause of adverse events. It was construed that under-reporting, though substantial, does not occur to the same extent for all medications and all events; common and non-serious events are more likely to be under-reported than serious or rare events. They pointed out that this state of affairs is auspicious to pharmacovigilance since rare or hitherto unknown but serious adverse reactions are wont to appear in 'remarkably' higher numbers in the spontaneous reporting system prompting extra scrutiny [33]. The problem with this situation is that it may lead to overlooking new adverse reactions which have attributes similar to frequently occurring adverse reactions or diseases [17,19]. The same can be said for adverse reactions whose characteristics are suggestive of the disease being treated [34]. Moore et al. [34] report that the spontaneous reporting system appears to be unable to detect that flecainide and encainide could occasion cardiac arrest nor could it discern that flosequinan use in the treatment of congestive heart disease could lead to increase in mortality.

Reporting of erroneous or partial information on adverse events is quite common. Affected variables include age, gender, dose, cotherapy and suspect medication. Indication, duration of treatment and disease and medical state of patients, are also affected [32,35]. Reporting practices and conventions are not uniform across countries or regions of the same country, health personnel and reporting institutions; which militate against the optimal use of the system [19,32,35].

The reporting rate of adverse events does not follow any clear pattern. The public could be inadvertently worked into a reporting fervour by the media if the latter overly focus on instances of adverse events, leading to uneven intervals of time during which reporting increases. It is thought that the marketing activities of

pharmaceutical concerns too impinge on the reporting rate from time to time. Moreover, regulation requirements may influence reporting. Reporting institutions are enjoined to be vigilant with uncommon and serious events, and this could unduly accentuate the reporting rates of such events [19,32,33,35].

There are instances of duplicate reports of the same adverse incidents as different entities (patient, medical personnel or sponsor), may report on the same adverse event episode or old cases are misrepresented as new owing to inappropriate tracing of events [35,36,37]. It is almost impossible to estimate the number of people using a given medication at any point in time.

Incidence rate and prevalence rate of adverse reactions are almost impossible to estimate owing to the inadequacies identified above [19,32,33]. It must be understood that the occurrence of an event during the use of a medication does not mean there is a causal relationship between the medication and the event. The occurrence of the event may have been accidental, or the event is related to the disease being treated or an unrecognised disease. Another medication or drug-drug interaction may have been responsible for the occurrence of the event [12,17,36], as it occurs when rifampicin and isoniazid are administered simultaneously [12].

### **2.3.2 Beyond the problems of spontaneous reporting system**

In spite of the difficulties enumerated above, the system has been very useful in recognising some adverse events as bona fide adverse reactions, in situations where identifying the reactions as such would have been more challenging or would have required more time, without the involvement of the system [26,34,35]. The spontaneous reporting system played a central role in establishing the link between the side effects of liver damage, seizures and addiction, aplastic anaemia and blood disorders and the corresponding drugs: troglitazone, tramadol, felbamate and temafloxacin [34]. Other cases include "hyperglycaemia, diabetes and exacerbation of diabetes" induced by olanzapine (zyprexa) use; renal failure in the use of aristolochia; manifestation of tendonitis and tendon rupture occasioned by use of quinolone antibiotics; and "serious cardio vascular reactions" brought on by cisapride (prepuisid,

alimix) use [26], which led to various regulatory actions. The Yellow Card Scheme helped to identify at least 26 drug safety issues from September 2013 to September 2016 [38] and at least a recommendation on educating health workers on the right dose for anti-snake venom was made to the respective Market Authorization Holders by the FDA (Ghana) following 11 adverse event reports it received in 2016 [28].

It is important to point out that pharmacovigilance is not exclusively conducted through the spontaneous reporting system. Any avenue capable of facilitating the determination of whether or not there is a causal relationship between an ADE and a suspect medication can be employed. Other means which have proven helpful include cohort and case-control studies using data from case registries and health facilities, vital statistics and information from the pathologist or coroner, and laboratory and tolerability data from clinical trials [1,17,19]. The spontaneous reporting system, nonetheless, remains most treasured because of the frontline role it has assumed. The other means are viewed as complementary to the SRS in causality assessments [27,32].

## 2.4 Justification for Participatory Pharmacovigilance

A complete health delivery system is one that pays the required attention to preventive health care as it should to the curative. According preventive health care due consideration ensures that: discomfort, pain and avoidable deaths caused by diseases and iatrogenic problems are curtailed or eliminated; the huge monetary cost and time required to deal with diseases and iatrogenic problems are avoided; other areas of the economy could then benefit from the time and funds saved [2].

Health fields as epidemiology and pharmacovigilance have come into being in recognition of this reality. A major challenge and preoccupation of pharmacovigilance is making timeous detection of unknown adverse drug reactions and other irregularities associated with drug use possible [2]. This, if achieved, will lead to the benefits mentioned above through:

- i. “Reduced morbidity, sick leave days and impaired days
- ii. Reduced potential liabilities
- iii. Reduced mortality
- iv. Less need for hospital capacities

- v. Reduced number of hospital stays and outpatient care” [39].

Some studies on ADRs are highlighted here in a bid to draw attention to the burden ADRs in general and unknown ADRs pose, and the need for all to be actively involved in reporting AEs accompanying drug use, even if the drug is only suspected to have caused the adverse event:

A research on ADRs in the US concluded that ADRs are a “leading cause of death in the United States” [34,40]. Thirty-nine studies, traversing a period of thirty years, were examined in a meta-analysis that estimated that the number of people who got hospitalised in 1994 as a result of ADRs was over 1.5 million. Adverse drug reactions occurring during hospital stay for reasons other than ADRs and those resulting in death in that year were estimated to be over 700, 000 and 100, 000 respectively. Occurrence of ADRs amongst inpatients was said to be about 6.7% (95% CI: 5.2% – 8.2%) overall. A notable feature of the findings was that most of the adverse reactions happened at doses deemed to be acceptable in humans [40].

A UK study, published in 2004, spanning six months and involving two general hospitals and a population of 18,820 inpatients; established that the proportion of the admissions caused by ADRs was 5.2% and on the whole 6.5% of the cases related to ADRs. Adverse drug reactions accounted for a median length of stay of 8 days ( $Q_1 - Q_2$ : 4 – 18 days) with a corresponding bed capacity of 4%. It was estimated that the National Health Service could incur a cost of £466 million annually due to ADRs [14]. In another study of the same duration as above, undertaken in the UK, and by two of the researchers involved in the above study; which focused on ADRs occurring during hospital stay, the prevalence rate of ADRs was estimated at 14.7%. Adverse drug reactions caused longer stay at the hospital for 26.8% of the patients, and the accompanying direct cost to the National Health Service as a result of the ADRs was projected to be £637 per annum. The authors noted that the direct cost was carefully determined and the estimated value was in consonance with estimates made in the US and mainland Europe [13].

Two related enquiries that examined the frequency and cost of ADRs and the possibility of preventing ADRs that result in hospitalisation, estimated that the direct cost to Germany due to hospital stay arising from ADRs was 1.05 billion

DM per year, based on an average inpatient cost per hospital day of 465 DM determined in 1995 [39,41]. The first enquiry examined 25 studies that were published in English or German and had been undertaken over the 25 years up to the year of the enquiry [41], and the second enquiry examined 13 studies published between 1975 and 1996 in English, French or German and covered a number of countries with comparable health delivery systems [39]. It was found that a median of 5.8% (Q<sub>1</sub> – Q<sub>2</sub>: 4.2 – 6%) of hospital admissions [41] and a median length of hospital stay of 8.7 (Q<sub>1</sub> – Q<sub>2</sub>: 8 – 12.3 days) [39] were caused by ADRs.

The WHO definition of an ADR, viz: “an adverse drug reaction is a reaction that is noxious and unintended and occurs at doses used for prophylaxis, diagnoses, or therapy of disease, or for modification of physiological function” [42] was used in the enquiries. While all the studies involved in the twin enquiries above were about ADRs, their focus, as one would expect, were not the same. Therefore it was difficult to thoroughly guarantee that each case of adverse event adhered to the definition, as pointed out by the authors [39]. A report on the second enquiry stated that 30.7% of hospital admissions

ascribed to ADRs were thought to be preventable [39]. Beijer and de Blaey [43] estimated avoidable ADRs to be 28.9% ( $\pm$  0.02) in a meta-analysis that involved 12 studies. It follows that the cost referred to in the twin enquiries, and perhaps that for the studies presented early on, almost certainly involved cost due to medications being used irregularly or inappropriately. As the foregoing narratives demonstrate, the problem of ADRs, including unknown but serious ones, is a huge one. Indeed the problem posed by unknown but serious ADRs cannot be underestimated as the remaining 70% or so of the hospital admissions which are attributable to bona fide ADRs cannot be ascribed to known ADRs alone [2].

Cost assessments from several studies that were concerned with ADRs that resulted in hospital admission and ADRs that occurred while on admission and the corresponding direct cost and length of stay over the last two and half decades, show that ADRs are a relentless drain on the economy [13,14,44,45,46]. Table 2 shows some annual cost estimates due ADRs that occurred while on admission or that resulted in hospitalisation.

**Table 2. Estimated cost of hospitalisation due to ADRs for selected ADR studies**

Setting	Cost per annum (millions)	Cost reference year	Affected country
Meta-analysis of 13 studies	DM 1050	1995	Germany [39].
Meta-analysis of 69 studies	£380	1994 – 1995	England [47].
Meta-analysis of 68 studies	£110 – £256	2000 – 2001	Netherlands [43].
National hospital data	> €226	2001	Spain [49].
A major teaching hospital	> £637	2005	England [13]
National hospital data	> €272	2006	Spain [49].

**Table 3. A sample of drugs withdrawn from marketing or distribution over the years.**

Drug name	Safety concern	Year withdrawn	Country concerned
Phenformin (DBI)	Lactic Acidosis	1978	US [27].
Flosequinan (Manoplax)	Excess mortality	1993	UK, US [27,52].
Bromfenac (Duract)	Hepatotoxicity	1998	US [27].
Troglitazone (Rezulin)	Hepatotoxicity	2000	US, Germany [27,53]
Rapacuronium Bromide (Raplon)	Bronchospasm	2001	US [27].
Cerivastatin Sodium (Baycol)	Rhabdomyolysis	2001	Worldwide [26,27].
Rofecoxib	Thrombotic Events	2004	Worldwide [53,54].
Valdecoxib (Bextra)	Heart Attack and Stroke	2004/2005	US, EU [53,54].
Rimonabant (Acomplia)	Psychiatric Disorders	2008	EU [54].
Rosiglitazone (Avandia)	Cardiovascular Disorders	2010	EU [54].

The settings of the studies that have attempted to gauge the magnitude of the problem of ADRs are not the same and so different methodologies and metrics were used in evaluating the problem. There is, therefore, no commonly accepted position on the extent of the problem of ADRs [46,48]. There is, nonetheless, a universal recognition that the problem is a huge one. The extent of the medical and socioeconomic burden ADRs present becomes even starker when indirect cost – cost arising from misconduct, injuries and intangible cost to patients; liability, claims or litigation costs – which were excluded from the studies are considered [39,48].

The exigency of doubling the effort at finding unknown but serious ADRs and curtailing if not eliminating preventable ADRs is amply demonstrated by a 1990 report on FDA's (US) drug review process for the period of 1976 – 1985, which indicated that drugs which were granted marketing approval with unknown side-effects constituted more than half (51.5%) of the total number approved for the period [50]. For the period of 1992 to 2002, a minimum of 12 drugs were subjected to regulatory action of one form or the other in the UK as a result of side-effects which were not known at the time of approval [51]. Safety issues discovered after approval resulted in the withdrawal from marketing or distribution of 24 drugs in the period of 1978 – 2001 in the US [27]. Table 3 shows some of the drugs withdrawn from the market or distribution over the years as a result of safety concerns that arose after market authorisation. The steady stream of safety information that are issued by the FDA (Ghana), FDA (US), MHRA & CHM (UK) and other regulatory bodies confirm the belief that the state of affairs with regard to ADRs would have been worse if regulatory bodies have not been performing the function of ensuring medications that could be potentially unsafe are not allowed on the market [2].

### 3. CONCLUSION

A number of considerations go into addressing the problem of ADRs and other irregularities associated with the use of drugs: ensuring that avoidable ADRs are prevented from occurrence, curtailing unavoidable ADRs, searching for ADRs that have not as yet been discovered, especially those relating to new medications and formulating specific solutions to deal with other medication irregularities [2]. In all these approaches reliable data is key. Granted that, in some respects, adverse drug effects and some

of the problems associated with drug use are unavoidable, we must strive to limit their occurrence and achieve a favourable risk-benefit ratio for medications through effective and efficient management of the irregularities and risks that come with drug use [2]. We need data of sound integrity to be able to achieve this health imperative. Improving the quality of data regulators work with will make it relatively easy for them to tease out patterns relating to counterfeited or substandard medicinal products, untoward effects of drugs, drug misuse or abuse or inappropriate use of drugs, where they exist; and thereby facilitate the fashioning of the most appropriate regulatory measures to address them. We can accomplish this if we address the problems of SRS enumerated above, most of which can be dealt with if all play an active role in not only reporting occurrences of adverse drug events and irregularities associated with drug use, but also ensuring that the correct information on all required variables are supplied as much as practicable and in good time. The FDA (Ghana) received about 57 ICSRs per million inhabitants for 2016, given the total number of ICSRs it received and the estimated size (28,308,301) [52] of Ghana's population for the year. Compared to the 200 or more ICSRs per million inhabitants per year done by countries within the higher segment of reporting rate [53], there is room for improvement.

### CONSENT

It is not applicable.

### ETHICAL APPROVAL

It is not applicable.

### COMPETING INTERESTS

Author has declared that no competing interests exist.

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