efavirenz. In four scenarios we explore changes in procurement modality and/or national first-line regimen (Table 1). In this example, we assume that the change in procurement modality is from one that requires quality assurance to one that does not, while a change in regimen includes introduction of a new medicine class without any resistance. Although there may be differences in magnitude of effects with careful quantification, this exercise suggests that regimen and procurement changes have the potential to affect acquired drug resistance.

While pharmacovigilance is dedicated to monitoring adverse events of medicines, passive and active surveillance systems will also be useful in monitoring medicine availability, quality, and effectiveness during regimen and procurement changes [10]. Passive surveillance relies on providers to report suspected substandard and falsified medicines, perhaps because of lack of therapeutic effectiveness in patients, while active surveillance requires testing the therapeutic quality of medicines. Strengthening and implementing national surveillance systems may help ensure timely detection of substandard and falsified ARVs.

Notes

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Reply to Suthar et al

TO THE EDITOR—We agree with Suthar and colleagues that substandard and falsified antiretrovirals (ARV) could affect the efficacy of antiretroviral therapy (ART) and promote the emergence and spread of human immunodeficiency virus-1 (HIV-1) drug resistance. Rigorous quality control of the ARV supply will ensure appropriate ARV exposure to both maintain viral suppression and minimize ARV-related toxicities. A key unanswered question is the range of ARV exposures across large populations of individuals that maintain both efficacy and safety. A recent study of cumulative ARV exposure, measured by their levels in hair samples, showed that a broad range of ARV exposures are compatible with sustained suppression of HIV-1 [1].

Suppression of HIV-1 replication in infected individuals is critical for limiting the HIV epidemic and is integral to the 90:90:90 goals set by the World Health Organization. One of these goals is for

90% of all people receiving ART to have viral suppression by 2020 [2]. There is a sizable gap between current rates of viral suppression and the 90% target. Complex interplay of multiple factors contributes to this gap, although pragmatic solutions have been offered and are being implemented [3]. Substandard ARV likely contributes to the suppression gap but could be addressed by improvements in quality control of ARV supplies.

Complete viral suppression is essential to prevent the emergence and spread of HIV-1 drug resistance. In some areas of South Africa, transmitted drug resistance is already at high levels (>10%; [4]), which reduces the efficacy of first-line treatment. In addition, 10%–30% of individuals experience virologic failure on first-line ART [5] and substandard ARV would be expected to increase failures. This undesirable outcome, in turn, would increase the number of individuals requiring more complex and expensive second-line regimens. Substandard ARV formulation could also adversely increase exposure to ARVs, causing toxicities such as renal or liver dysfunction. Greater toxicity could result in poor treatment outcomes and major additional costs to the national health systems that are already stressed.

In closing, we concur with Suthar et al [6] that as transition to country procurement of ARVs increases, it is imperative that country-specific guidelines be developed to monitor the quality of medications being procured. These guidelines should cover both initial and on-going procurement and logistical requirements to ensure that a steady supply of high-quality ARVs is available for individuals on therapy. As countries move to new ARV regimens, these guidelines would also ensure that the transition occurs without loss of quality. A further quality control measure would include sampling of individual ARV levels at primary health care facilities in comparison to expected exposures. Therapeutic drug monitoring has not been a feature of the care of HIV-1-positive individuals and

its main use has been in clinical trials to assess adherence. There are circumstances, however, in which measuring drug concentrations could be useful for individual patient management, including assessment of continued viremia on ART and monitoring ARV exposure during pregnancy to optimize prevention of maternal-to-child transmission, and during preexposure prophylaxis to prevent HIV-1 acquisition. To these ends, there are ongoing efforts to develop point-of-care semiquantitative tests to measure drug levels (particularly tenofovir). Such efforts could help determine if ARVs from new suppliers produce the expected drug levels in blood.

Note

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Caution Indicated in Extrapolating Carditis in Rats to Rheumatic Heart Disease in Humans

TO THE EDITOR—The article by Sikder et al [1] demonstrated that repeated injections of killed group G streptococci (GGS) or its purified M protein induced an autoimmune carditis in a rat model. The authors concluded that acute rheumatic fever and