

Investigation of the quality of cytotoxic anticancer medicines in five Tanzanian hospitals

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The quality of injectable cytotoxic anticancer medicines available in Tanzanian healthcare facilities was investigated, encompassing ten active pharmaceutical ingredients (APIs): carboplatin, cyclophosphamide, docetaxel, doxorubicin, etoposide, fluorouracil, ifosfamide, methotrexate, oxaliplatin, and vincristine. A total of 88 samples were collected from five Tanzanian hospitals. An additional 12 samples representing the same APIs were sourced from Germany for comparison and to support method development. The identity and quantity of the APIs, and the excipient compositions were assessed using a Raman/UV spectrometer (QCRx; Icones Services, France) and/or HPLC, benchmarked against certified reference standards. To the best of our knowledge, this is the first time that Raman/UV spectroscopy has been used for the detection of substandard and falsified finished pharmaceutical products. Validation of this method according to the current ICH guidelines proved accuracy, precision, and specificity. The method ensures safety of the operators in the analysis of cytotoxic medicines, is rapid and also allows the identification of excipients that are not readily accessible to HPLC analysis.

Among the 88 samples collected in Tanzania, the declared API was confirmed in all cases; however, 11 samples (12.5%) fell outside USP content specifications. One doxorubicin vial exhibited insufficient API content (85.2% of the declared amount), while for ten samples excessive API levels were measured. The latter included all six samples

of one ifosfamide brand (measured to contain 112.7–119.8% of declared amount) and both samples of one cyclophosphamide brand (122.3 and 129.1%). Additionally, one vincristine product was considered as non-compliant due to an extreme inconsistency in the concentration of the preservative methylparaben (1.0 vs. 0.15 mg/mL across different vials of the same batch). Declaration of excipients was found to be incomplete for 20 of the 50 brands examined, with undeclared substances — including urea, mannitol, methyl- and propylparaben, and Tris-HCl — detected analytically.