

### **c. FDA Adverse Event Reporting System Review**

A review of the FDA Adverse Event Reporting System (FAERS) was performed to characterize a constellation of symptoms leading to disability that had been observed during FDA monitoring of fluoroquinolone safety reports. This constellation of symptoms will be referred to in this review as “fluoroquinolone-associated disability” (FQAD). While most of the individual AEs that exist within FQAD are currently described in fluoroquinolone labeling, the particular constellation of symptoms across organ systems is not. Individuals with FQAD were defined as U.S. patients who were reported to be previously healthy and prescribed an oral fluoroquinolone antibacterial drug for the treatment of uncomplicated sinusitis, bronchitis, or urinary tract infection (UTI). To qualify, individuals had to have AEs reported in two or more of the following body systems: peripheral nervous system, neuropsychiatric, musculoskeletal, senses, cardiovascular, and skin. These body systems were chosen as they had been observed to be frequently involved with the fluoroquinolone reports describing disability. In addition, the AEs had to have been reported to last 30 days or longer after stopping the fluoroquinolone, and had to have a reported outcome of disability.

The regulatory definition of disability was used for this review, i.e., “a substantial disruption of a person's ability to conduct normal life functions,” (21 CFR 314.80: Postmarketing reporting of adverse drug experiences). Whether a case report met a legal definition of disability was not a consideration for this review, and FQAD should not be construed to represent a legal definition of disability. A “healthy patient” was defined as a person able to perform all of the usual activities of daily living without significant restrictions prior to taking the fluoroquinolone. Patients were included if they had controlled disease states, such as hypertension, hypothyroidism, or hyperlipidemia.

The FAERS database was searched with the strategy described in Table 3.

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