The American Society of Regional Anesthesia and Pain Medicine's Third Practice Advisory on local anesthetic systemic toxicity is an interim update from its 2010 advisory. The advisory focuses on new information regarding the mechanisms of lipid resuscitation, updated frequency estimates, the preventative role of ultrasound guidance, changes to case presentation patterns, and limited information related to local infiltration anesthesia and liposomal bupivacaine. In addition to emerging information, the advisory updates recommendations pertaining to prevention, recognition, and treatment of local anesthetic systemic toxicity. WHAT'S NEW IN THIS UPDATE?: This interim update summarizes recent scientific findings that have enhanced our understanding of the mechanisms that lead to lipid emulsion reversal of LAST, including rapid partitioning, direct inotropy, and post-conditioning. Since the previous practice advisory, epidemiological data have emerged that suggest a lower frequency of LAST as reported by single institutions and some registries, nevertheless a considerable number of events still occur within the general community. Contemporary case reports suggest a trend toward delayed presentation, which may mirror the increased use of ultrasound guidance (fewer intravascular injections), local infiltration techniques (slower systemic uptake), and continuous local anesthetic infusions. Small patient size and sarcopenia are additional factors that increase potential risk for LAST. An increasing number of reported events occur outside of the traditional hospital setting and involve non-anesthesiologists.