Table 1. Major Events That Created and Alleviated Ascorbic Acid Injection Shortages in the US

Date	Event	Affect on Availability of Ascorbic Acid Injection (AAI)	Result
10/1998	Steris Laboratories, the only manufacturer of AAI, signed a Consent Decree of Condemnation and Permanent Injunction that prevented future manufacturing of AAI.	Immediate and critical AAI shortage without warning. Manufacture of all AAI ceased. Manufacturer recalled all AAI produced.	Significant AAI Shortages. There were few compounding pharmacies producing sterile drugs in 1998.
10/1999	Multiple compounding pharmacies begin producing AAI.	Gradual improvement in AAI availability.	AAI is generally available and office use is common.
4/2002	McGuff Pharmaceuticals, Inc. begins AAI manufacturing and distribution.	AAI is sold as a grandfathered commercial drug product. Multiple manufacturers enter market.	AAI is available in quantities needed. AAI is available from manufacturers and a few compounding pharmacies.
6/2006	FDA publishes *Guidance for FDA Staff and Industry Marketed Unapproved Drugs – Marketed New Drugs Without Approved NDAs or ANDAs*.[2]	Possible immediate effect of removing AAI as a manufactured drug. No warning required.	FDA warns industry that drugs marketed without approval may be removed from market. AAI does not have NDA or ANDA approval.
12/2010	FDA declares AAI is not a grandfathered drug and is not an approved drug. Manufactured AAI is recalled by all manufacturers except Mylan. FDA uses its enforcement discretion to allow Mylan to continue to import and sell AAI in US. All US manufacturers remove themselves from US market.	Immediate and critical shortage without warning. US AAI manufacturing shut down.	Loss of all manufactured AAI in US except Mylan's limited production. Compounding pharmacies gradually re-enter market. Mylan, realizing they have FDA enforced monopoly starts raising AAI price.
9/2012	New England Compounding Center meningitis outbreak sickened 753 individuals and resulted in the death of 64 due to fungal infections resulting from contaminated steroid injections.[3]	No immediate effect, AAI availability good.	FDA and State investigations lead to increased regulatory overview of compounding pharmacy.
11/2013	Federal Drug Quality and Security Act adds significant restraints to pharmacy compounding, distribution, and requires individual prescriptions to obtain AAI. FDA starts to inspect 503(a) compounding pharmacies.[4]	Gradual loss of AAI availability. Nineteen FDA draft and final guidances on compounding pharmacy published since July 1, 2014 put extraordinary pressure and uncertainty on compounding pharmacies.[5]	As compounding pharmacies leave sterile drug market AAI becomes more difficult to obtain. Complex procedures required for prescription ordering and production.
2/2015	FDA Draft Memorandum of Understanding Addressing Certain Distributions of Compounded Human Drug Products Between the State…and the US Food and Drug Administration[6]	No immediate effect but significantly detrimental to inter-state dispensing / distribution when enforced.	Combines the words dispense and distribute to mean distribute. Will limit interstate shipment of AAI (and all other compounded drugs) to five or 30 percent of all drugs compounded per month.
12/2016	FDA Final Guidance, Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act	Additional restrictions on compounding pharmacies, e.g. compounding in anticipation of prescription.	Further complicates a compounding pharmacy's ability to produce appropriate quantities of AAI.
10/2017	McGuff Pharmaceuticals receives approval of NDA 209112 for Ascor® (Ascorbic Acid Injection).[7,8]	AAI as an approved drug will be manufactured now and into the future.	Eliminates AAI dependency on compounding pharmacy and outsourcing facility law and regulations. Eliminates need for prescriptions that are required for compounding. Eliminates office use restrictions.