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USS Thresher (SSN 593) was lost 10 April 1963 off the New England coast. All 112 naval personnel and 17 civilians aboard were killed. The vessel was on post-overhaul trials, operating from Portsmouth (NH) Naval Shipyard. The submarine was in communication with a surface vessel during her loss. It is believed that her reactor shut down during deep diving trials; she then attempted to blow her tanks to surface, and the expanding air from the tanks froze the air lines. She could not surface with the reactor shut down (reportedly it would take 45 minutes to restart such a reactor) and the air lines frozen. The cause of the reactor shutdown is not known. Thresher was crushed by water pressure as she sank. USS Mizar (AGOR 11) located the wreckage of the submarine in 1964; the site has been surveyed several times since then.

USS Scorpion (SSN 589) was declared lost 6 June 1968. It was determined (presumably by examination of SOSUS tapes or other evidence) that she was lost on 22 May 1968, 400 miles southwest of the Azores. All 99 men aboard perished. Like Thresher, she was crushed by water pressure as she sank. Mizar located the remains of the submarine; the site has been surveyed several times. Scorpion was carrying nuclear weapons at the time of her loss.

The exact cause of the loss is not publicly known. If the Navy has determined the cause, they've kept it secret. The most popular theories involve some form of torpedo malfunction, with resulting internal or external explosion, but there is continued debate and discussion on this issue. It is likely that the cause will never be known with certainty.