The Snake River is named for the Snake Indians, through whose country the greater part of the river flows. The Indians, in turn, were named "Snake" by their Plains neighbors to the east, possibly because they reputedly used snake heads painted on sticks to terrify their Plains enemies. (At least the Blackfeet on upper Bow River reported finding such Shoshoni snake sticks in about 1784.) Or possibly the sign employed to designate the Snake Indians in conventionalized sign language—a snake-like motion—may have suggested the name to the Plains Indian. In any event, the name used to identify the Snake Indians in various Plains Siouan languages was the word for snake or rattlesnake. The French picked up the name from the Plains Indians, and the British, in turn, translated it from the French.

French fur traders in Louisiana, having assumed the existence of what in fact turned out to be the Snake River opposite the head of the Missouri, planned to search for that stream throughout much of the earlier eighteenth century. Their theory was that such a river ought to give them convenient access to the Pacific. The most advanced French expedition toward the upper Missouri struck southwest from that river in North Dakota in 1742, accompanying a band of unidentified Plains Indians who were on their way to have a war against their dreaded enemies, the Snakes. The French party—the Verendrye party—had come along because the Snakes were thought to live on both sides of the Continental Divide. Moreover, the Indians assured Verendrye, the waters of the Pacific were plainly visible from a high mountain in the Snake country. The Snakes seem to have fled from the Indian party whom the Verendrye expedition accompanied; but upon observing that, Verendrye's Indians also took off in a panic, fearing that the Snake flight was actually a movement to cut off their rear supply camp. Verendrye thus had to return east without reaching the Continental Divide as he had hoped.

French efforts to make contact with the Snake Indians and to explore their country were resumed at the end of the eighteenth century. In 1794, Jean Baptiste Truteau was sent out with instructions to do just that, in preparation for a French expedition to reach the Pacific by the upper Missouri. Truteau did not get to the Snake country; and before the French had reached the Pacific via the projected Missouri-Snake River route, Louisiana was transferred to the United States. Lewis and Clark accomplished what the French had set out to do; in the process, they found the Snake River, although they did not call it that.

In the next few years, upper Snake River was explored by Andrew Henry, who established a winter post on Henry's Fork in 1810, and by the Wilson Price Hunt Astorian expedition the next year. Hunt, knowing of no name for the Snake River, decided hopefully to
call the stream "Canoe River." That name, however, turned out to be entirely inappropriate. In 1812, Robert Stuart noted that "the generality of whites" referred to the stream as the Snake River, and that is the name that lasted.