Vaccine development targeting *Vibrio cholerae*

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At the first "Vibrios in the Environment" conference in 1980, the initial molecular genetic studies were being performed on vibrios. The cloning of the genes encoding cholera toxin (*ctx*) quickly led to the construction of attenuated *Vibrio cholerae* strains in which the *ctx* genes were specifically mutated. The original belief was that simple elimination of cholera toxin by deleting the *ctx* genes would yield a safe and effective *V. cholerae* vaccine strain that would provide protection against cholera. The first *Δctx* strains engendered strong protective immunity when tested in volunteers but were unexpectedly reactogenic, causing mild to moderate diarrhea in a number of subjects even in the absence of cholera toxin. Further attenuated strains were developed that were well tolerated and immunogenic in a single dose, including CVD 103-HgR and Peru-15. CVD 103-HgR was licensed for human use and sold in several countries throughout the world but is not currently being manufactured. An alternative approach to cholera vaccine development is the use of killed whole organisms administered orally in two or more doses. One such vaccine, Dukoral, contains recombinant purified cholera toxin B subunit in addition to whole cell antigens and is currently available in several countries. A newer version of the killed whole cell vaccine called Shanchol lacks the purified B subunit and is substantially less expensive than Dukoral.