Several publications disclose *C. difficile* vaccines. Vaccines wherein TcdA and TcdB are incativated by the chemical agent formalin are disclosed in Sougioultzis S. L. et al., Gastroenterology (2005), 128:764-770; Kotloff, Infect. Immun. 2001; WO9920304, and Ghose et al, Infect. Immun. (2007), 75(6), 2826-2832. Vaccines comprising recombinantly expressed polypeptides representing the C-terminal ligand domain of TcdA or TcdB are disclosed in WO9859053, WO0061761, WO0061762, WO9702836, Pavliakova et al, Infect Immun (2000), 68(4), 2161-2166; Ward et al, Infect Immun (1999), 67(10), 5124-5132; and Lyerly et al., Current Microbiol 21: 29-32). WO2007146139 discloses a codon-optimised DNA-molecule encoding the receptor binding domain of TcdA and TcdB and is use as a DNA vaccine. WO2004041857 discloses non-toxic mutants of TcdB and its use for vaccination. Genth, H. et al., Infect. Immun. (2000), 68: 1094-1101 discloses a method to generate enzymatically deficient *Clostridium difficile* toxin B as an antigen for immunization.

Vaccines are typically manufactured by making a preparation comprising antigenic components of such pathogens and admixing them with a pharmaceutically acceptable carrier. To achieve an effective immune response and for economic reasons it is desirable to use preparations obtained from bacterial cultures with only few processing or fractionation steps. In the case of toxin producing organisms, the problem is that the toxins included in such preparations would prevent administration thereof unless they are inactivated. Therefore, the prior art approaches have suggested to make vaccines against bacterial pathogens producing AB toxins like *C. difficile* by chemical inactivation of the toxins, recombinant expression of the non-toxic domain of the toxins (the C-terminal receptor binding or "B" domain), or producing non-toxic mutants of the toxins. However, all these measures lead to a loss of antigenic epitopes of the pathogenic organism which may affect the effectivity of the vaccine, and/or are costly.

BRIEF SUMMARY ~~OF THE INVENTION~~

The present disclosure~~invention~~ relates to a process for the production of a vaccine against bacterial pathogens which produce an AB toxin, comprising

(a) Culturing the pathogen under conditions where the AB toxin is produced, and harvesting the culture;

(b) Cleaving the AB toxin enzymatically *in vitro*; and

(c) Combining the composition of step (b) with a pharmaceutically acceptable carrier.

In a first aspect, there is provided a process for the production of a vaccine against bacterial pathogens which produce an AB toxin, comprising (a) Culturing the pathogen under conditions where the AB toxin is produced, and harvesting the culture; (b) Cleaving the AB toxin enzymatically *in vitro* wherein inositol phosphate is used as a co-factor; and (c) Combining the composition of step (b) with a pharmaceutically acceptable carrier.

In an embodiment~~a preferred aspect~~, the enzymatic cleavage is autocatalytic. In another embodiment~~a preferred aspect~~, inositol phosphate, preferably inositol hexaphosphate is used as a co-factor of the enzymatic cleavage.

In another embodiment~~a further preferred aspect~~, the disclosure~~invention~~ relates to a process as described, wherein the cells are separated from the culture medium after the harvest, and the AB toxin in the culture medium is cleaved.

The process of the disclosure~~invention~~ can be used for the production of vaccines against pathogens of the genus *Clostridium*, preferably *C. difficile*, *C. sordellii*, *C. botulinum*, *C. perfringens*, *C. tetani*, or *C. novyi*, or of the genus *Vibrio*, preferably *V. cholerae*, *V. parahaemolyticus*, *V. vulnificus*, or *V. splendidus*, or *V. anguillarum* or of the genus *Xenorhabdus*, preferably *X. nematophila*, *X. bovienii*, or of the genus *Yersinia*, preferably *Y. pseudotuberculosis*, *Y. pestis*, *Y. enterocolitica*, or *Y. mollaretti*, or of the genus *Bordetella*, preferably *B. pertussis*, *B. parapertussis*, or *B. bronchiseptica*, or of the genus *Actinobacillus*, preferably *A. pleuropneumoniae*, or *A. suis* and *E. coli*.

An adjuvant may be added to the vaccine composition.

In a further aspect, there is provided~~the present invention relates to~~ a vaccine produced with the process as described.

In a further aspect, there is provided a vaccine against *Clostridium*-induced diarrhoea, comprising Toxoid A and/or Toxoid B of *Clostridium difficile*, wherein said Toxoid A and/or Toxoid B has been generated from Toxin A and/or Toxin B by autocatalytic cleavage, optionally together with a pharmaceutically acceptable carrier.

In a further aspect, there is provided a vaccine produced as defined above for use in the vaccination of animals, including humans, against infection of pathogens producing AB toxins.

In a further aspect, there is provided the use of a vaccine produced as defined above in the preparation of a medicament for the vaccination of animals, including humans, against infection of pathogens producing AB toxins.

The disclosure also relates~~Another aspect of the invention is related~~ to the use of a vaccine produced according to the process as disclosed, for the vaccination of animals, including humans, against infection of bacterial pathogens producing AB toxins.

The disclosure also~~Another aspect of the invention~~ relates to a method of vaccination of animals, including humans, against infection of bacterial pathogens producing AB toxins, comprising administering an effective amount of a vaccine produced according to the process of the invention to an animal, including a human.