Nonclinical evaluation of adjuvants and adjuvanted vaccines. Background of the WHO-guideline.

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The WHO took the initiative of writing a guideline on the nonclinical evaluation of vaccine adjuvants and adjuvanted vaccines. The EU guideline on adjuvants became in force in 2005, and several adjuvants came on the market since then. With this experience and new insights on the impact of Toll-like receptors on the immune responses, an update of the regulatory testing was needed, preferably from a global perspective. After a consultation workshop in 2011, a drafting group consisting of experts on nonclinical testing from various regulatory areas in the world (Indonesia, Canada, United States, Europe) was established. Important topics being discussed were the testing of the adjuvant independent from the antigen, the design of reproductive toxicity studies and a possible relation with the induction of autoimmunity.

It became clear that testing of the adjuvant alone is of limited value, and combination with an antigen in a single relevant species is to be recommended. With respect to reproductive toxicity it is clear that vaccination during pregnancy might be important to protect the mother as well as the child, but an adjuvant might be a risk especially very early in pregnancy. Recommendations for an adapted study design have been given. Autoimmunity has been suggested to be a specific risk for adjuvanted vaccines, and this has been discussed thoroughly. There is no compelling evidence, however, that there is an association between adjuvants and autoimmunity disease symptoms. Animal models are not present to support such relationships.