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Research Article

# Parameters of Adjuvant in the Safety Profile of Human Vaccines in Relation to Toxicity

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## Abstract

The adjuvants used for many years for increasing the immune response have been aluminum salt. This adjuvants fill out the conditions for safety and efficacy for increasing the immune response [1-4]. Adjuvants are characterized by several parameters that must be taken into consideration for the safety and efficacy of human vaccines. Some of the parameters that characterize adjuvants are critical and their identification is of particular importance. The identification of these parameters is done during the assessment of the quality of vaccines/adjuvants. During the assessment of the quality of vaccines, other parameters should also be included, which should be routine analyses. This assessment is very important because the quality, safety and efficacy of vaccines are related to the life and prevention of various infections of the population. The characteristic parameters of adjuvants depend on the nature of the adjuvants, which can be of chemical or biochemical composition [5].

**Keywords:** Adjuvant; Analysis; Toxicity; Safety; Benefit; Risk

## Introduction

The adjuvants are using in vaccines for increasing immune response especially for vaccines with poor immunogenicity [6].

Purity is related to the content of endotoxin, biological load and production residue.

Studies conducted in the field of vaccinology regarding their safety and efficacy have made it possible to develop many adjuvants. Some of the discovered adjuvants were never accepted for routine vaccination because they had problems with the safety of the vaccine, e.g. problems with acute toxicity. The decision to accept or not an adjuvant in our case is based on analyzing the benefit/risk ratio of each undesirable side effect.

The scheme for evaluating the benefit risk ratio will be as follows:

- Let's do an analysis of the benefits and risks of vaccine adjuvants.

The benefits of vaccine adjuvants are:

- Improved immunogenicity
- Saving vaccine doses, since immunity can be achieved more easily
- Effective vaccine in specific populations
- Broader and more durable protection
- All these benefits lead to the prevention of diseases [5].

## Material and Method

This study is based on effect of adjuvants for increasing of the immune response of vaccines and their safety related to the toxicity. In the manuscript are involved the results of safety of vaccines according to the parameters of adjuvants. Also is an analyzing for the benefit risk of the vaccines based on the adjuvants contents.

## Results and Discussion

Nowadays the technology advanced for the vaccines production, but also and concerned for the safety of these production is increased. We know the "vaccine hesitancy" which is spread worldwide.

This hesitancy encouraged during the COVID-19 pandemic. COVID-19 pandemic was the strong argument for the importance of the vaccines against infectious diseases, and in the other side also the hesitant behavior from the group of population. This hesitancy behavior is from a part of the population, and it is related to the side effects of the vaccines and the misinformation about the vaccines composition.

The choosing of the vaccines adjuvants should be considered the first of all the safety issues.

One good adjuvant will fulfill this condition:

- Should be safe
- Should be well- tolerated
- Should be easy to produce
- Should have good pharmaceutical characteristics like: osmolality, endotoxin levels, etc.
- Should have stable shelf life over time
- Should have low cost for production [2].

In the case of injecting vaccines into healthy people, the benefit/risk ratio of vaccination, the safety of the vaccine is the main one compared to the effectiveness of the vaccine. If we have patients with high health risks affected by cancer or AIDS infection, a high level of toxicity may be acceptable if the use of the vaccine brings significant benefits. These vaccines are called "therapeutic vaccines". However, the surveillance of Adverse Events Following Immunization (AEFI) continues even if no serious adverse effects are observed in the non-clinical toxicological safety study. This surveillance is necessary because it cannot be guaranteed that the new formulation of the vaccine/adjuvant cannot guarantee absolute safety, because unexpected situations can occur.

The most important benefit of the adjuvants used in the production of vaccines is the increase of the immune response. Other benefit is the decrease of the doses of the vaccines used for the immunization of the population. This decreasing number of the doses not only is comfortable for the patient, but also save budget and protect the environment from the vaccination waste.

The group of population which is problem the immune response from vaccination, adding of the adjuvants will improve their immunity. It is for the people infected with HIV- AIDS ect.

All these benefit help prevention of infected diseases.

Studying the risk of adjuvants are reported some local reaction which occur soon after vaccination and include redness, swelling or induration at the injection site, as well as systemic symptom [7].

### Combined adjuvants

The combination of antigen and adjuvant is a very critical point related to the biological properties of the agent/adjuvant such as adsorption, binding characteristics, identification and monitoring. If a combination of several adjuvants is required to increase the efficacy of the vaccine, then the necessary information should be studied and obtained for each adjuvant and antigen in detail.

In the case of a combination, it will be sufficient to compare the combination without adjuvant with the combination plus each adjuvant, and this early-stage study may provide information on safety, but this information is limited. The study will be conducted in healthy adults and in a relatively small number of individuals and should include a comprehensive assessment of the potential effects of adjuvants on the immune response to all antigens included in the final products. The number of tests for adjuvants depends on the nature of the adjuvants and antigens.

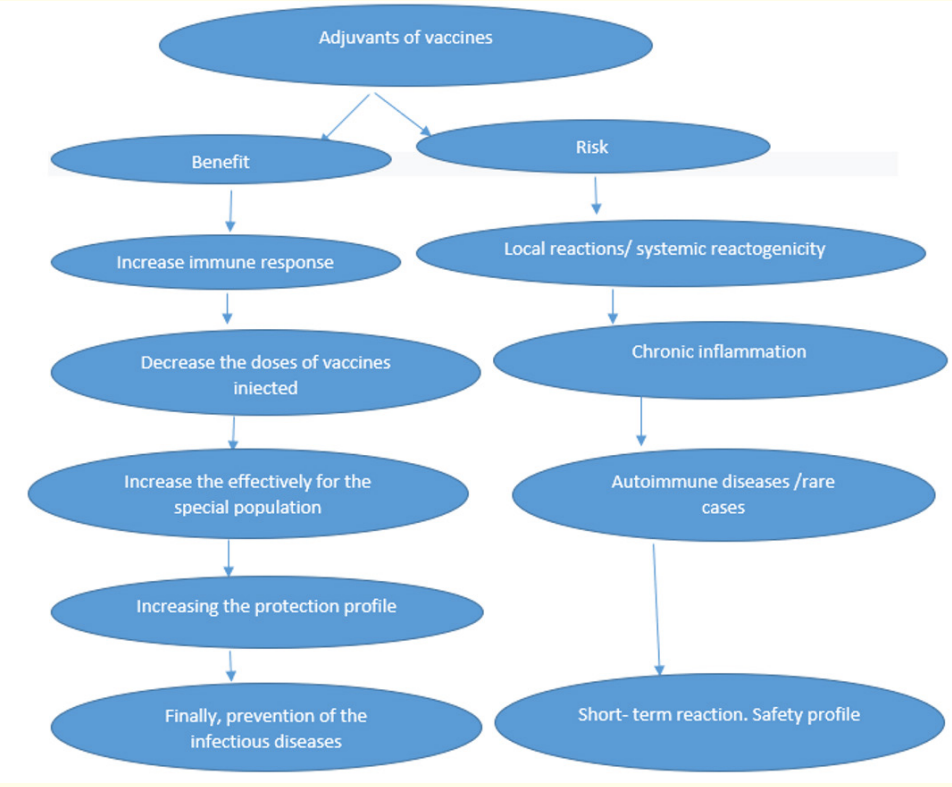


**Figure 1:** The scheme for study of benefit/risk for adjuvants of vaccines [7].

## Systemic toxicity

Adjuvants of different classes may be distributed systemically and may cause toxicity in different organs. Protocols should be designed to establish dose-dose relationships and include repeated administration at intervals that reflect the clinical use described in the protocol. Complete histopathology is also required, especially for primary and secondary immune organs. This dose control allows for control of toxicity, increasing the safety of vaccines.

## Reproductive toxicity

Vaccines can be administered to healthy women who may become pregnant after vaccination, or can be administered during pregnancy to prevent infectious diseases in the infant through passive immunization. To avoid toxicity and its effects, studies should be conducted on the adjuvants intended for use in this group of vaccines.

## Genotoxicity

Adjuvants can be derived from biological as well as synthetic origin. Genotoxicity studies for biologically derived adjuvants may not be considered relevant with toxicity. Studies have been conducted on cell lines regarding the genotoxicity of various forms of aluminum.

Some scientists have conducted ex vivo studies using lymphocytes donated by different donors, as well as embryo toxicity in animals.

The results of the studies were contradictory and inconsistent. These results indicate that aluminum salts used in certain doses as adjuvants in vaccines cannot be said to be toxic [5,7,8].

## Conclusion

- The adjuvants used for increasing immune response on human vaccines are not toxic and their characteristic fill out the conditions for safety profile
- Before using in human adjuvants for human vaccines tested in clinical trial and if the ratio benefit/risk is higher it will used in vaccine production
- Currently, from the results of clinical trial has no scientifically any explanation of the toxicity related to adjuvants.

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