

VACCINE ADDITIVES AND RESIDUALS



Nothing Is 100% pure

Background: With the exception of “eternal love” and “pure olive oil”, nothing exists in a “pure way”. From German beer, to tap water, to commercial drinking water to water used for medical injections: there are ALWAYS traces of contaminating substances. The overall concept is to avoid or reduce these to the lowest possible amount. Vaccine additives and residuals are carefully selected inactive components or trace process leftovers that improve vaccine stability, safety and effectiveness while remaining far below toxicological concern.

Main groups of additives

1 Stabilizers

- **Function:** Protect antigen structure during manufacturing, storage and transport (e.g., sugars, amino acids, gelatin, recombinant human albumin).
- **Key points:** Allow cold chain fluctuations, prevent aggregation; amounts are small compared with daily dietary intake and endogenous exposure.

2 Preservatives

- **Function:** Prevent microbial growth (e.g., thiomersal in some older or in multidose vaccines, 2-phenoxyethanol).
- **Key points:** Modern single dose vaccines are largely preservative free; past large studies show no link between thiomersal and autism or neurodevelopmental disorders.

3 Adjuvants (e.g., aluminum)

- **Function:** Enhance immune response, enabling lower antigen doses and longer lasting protection.
- **Key points:** EMA/FDA and recent reviews confirm a favorable benefit–risk balance; no evidence of neurotoxicity at vaccine exposure levels.



Residuals from manufacturing

1 Formaldehyde

- **Use:** Inactivates viruses and detoxifies toxoids (e.g., diphtheria, tetanus).
- **Exposure:** Endogenous daily production is hundreds of thousands of times higher than the maximal amount in a vaccine dose; remaining formaldehyde is rapidly metabolized.

2 Antibiotic traces

- **Use:** Prevent bacterial contamination during cell culture.
- **Features:** Allergenic antibiotics such as penicillin/streptomycin are not used; only trace amounts (if any) of others (e.g., neomycin) remain, mainly relevant for rare delayed local reactions.

3 Host cell DNA and proteins

- **Source:** Cell substrates (e.g., Vero, CHO, egg, insect cells) used to grow viruses or express proteins.
- **Levels:** Highly fragmented and present at nanogram or less levels per dose, well below WHO/EMA/FDA safety limits; no evidence of oncogenic effects in humans.

Excipients with allergy relevance

1 Egg proteins

- **Source:** Egg based production of influenza, yellow fever, TBE, and some other vaccines.
- **Practice:** MMR and TBE are highly purified and generally safe in egg allergic patients;
 - **severe egg allergy requires precaution for yellow fever and selected influenza vaccines.**
 - **cell culture–derived products available today for influenza**

2 Polysorbate 80 and gelatin

- **Role:** Prevent aggregation (polysorbate); stabilize formulations (gelatin).
- **Risk:** Rare causes of hypersensitivity; cross reactivity with PEG/polysorbates described in isolated cases, managed with allergy evaluation and tailored vaccination strategies.

3 PEG and lipid nanoparticles (mRNA vaccines)

- **Role:** LNPs (ionizable lipid, phospholipid, cholesterol, PEG lipid) deliver mRNA into cells.
- **Safety:** Nonclinical and clinical data show transient biodistribution and rapid clearance; anaphylaxis is very rare (a few cases per million doses) and largely attributable to PEG in predisposed individuals.

Emerging quality topics and safeguards

1 Nitrosamines and new impurities

- **Action:** EMA and FDA require formal risk assessments for nitrosamines across drug classes, including vaccines, even though no clinically relevant nitrosamine contamination has been documented in vaccines.

2 Analytical advances

- **Tools:** qPCR, next generation sequencing, LC MS/MS and orthogonal assays now characterize residual DNA, proteins and process related impurities with high sensitivity.
- **Outcome:** Confirms that residuals are extremely low and supports continuous tightening of specifications without compromising vaccine supply.

3 Risk communication

- **Focus:** Clear labeling, FAQs and professional guidance help address public fears about “toxins” by explaining that additives and residuals are present at tiny, controlled levels with strong regulatory oversight.

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