Attachment 2: Inclusion and exclusion criteria

Inclusion criteria	
***P**articipant* **(patient/proband)**	*Indication:* Prevention of infections with influenza-A- (H1N1 and H3N2) and -B in humans *Age:* Studies that included children up to 18 years of age
***I**ntervention* **(intervention/ exposure)[1]**	*Narrow:* Trivalent LAIV against influenza A-H1N1, H3N2 and -B, cold adapted; temperature-sensitive; attenuated master-donor viruses /Ann Arbor/6/60 and B/Ann Arbor/1/66. Application form: intranasal *Dosage:* Approx. 10^7 *fluorescent focus units* (FFU) per strain *Broad:* Any vaccine for the above indication
***C**omparison* **(comparative intervention)**	• Placebo • Non-vaccination • Other vaccines • Trivalent inactivated influenza vaccine (TIV)
***O**utcomes* **(target criteria)**	Medical section: *Efficacy:* • Laboratory-confirmed influenza infection • Quality of life (based on objective measurements or subjective reports) • Other patient-relevant endpoints *Safety:* • Number of study participants with at least one adverse event (AE) • Number of study participants with at least one serious adverse event (SAE) • Number of study participants with at least one AE resulting in the discontinuation of the study medication and/or withdrawal from the study • Other patient-relevant AE Epidemiological section: *Effectiveness:* • Mortality • Morbidity (including incidence of influenza cases, ILI/ARI and their complications, secondary diseases/complications) • Utilisation of the health care system (including visits to GP and hospital admissions) • Quality of life (based on objective measurements or subjective reports) • Other patient-relevant endpoints • Herd protection *Safety*: • AE in association with the influenza vaccination Economic section: • (Additional) costs per effect unit (e.g. additional years of life, prevented events, prevented deaths, gained QALY) • Cost savings and corresponding ratios

Attachment 2 to: Andersohn F, Bornemann R, Damm O, Frank M, Mittendorf T, Theidel U. Vaccination of children with a live-attenuated, intranasal influenza vaccine – analysis and evaluation through a Health Technology Assessment. GMS Health Technol Assess. 2014;10:Doc03. DOI: 10.3205/hta000119

	Ethical, social, legal considerations (ESL) Studies on health-related topics • Awareness • Perspectives • Preferences • Behaviour • Acceptance • Duty of information • Liability risks • (Human) rights • Children's rights • Parents' rights • Right to information • Right to safety/efficacy of medicinal products • Freedom of decision • Reimbursement of costs • Access barriers

Study type	Medical section:
	• RCTs and meta-analyses of RCTs
	• Re-analyses of RCTs (e. g. re-analyses in relation to a subgroup of relevance to the HTA)[2]
	• Meta-analyses are included if all data derive from relevant primary studies
	• In addition, HTAs and systematic reviews are captured as full-text versions for subsequent screening for further RCTs or meta-analyses of RCTs
	
	Epidemiological section:
	• Epidemiological studies (including cohort studies, case-control studies, prevalence studies, ecological studies, self-controlled designs)
	• Meta-analyses / meta-regression analyses of epidemiological studies
	• HTA reports
	• Systematic reviews
	
	Economic section:
	• All health-economic evaluation studies on the vaccination of children against (seasonal) influenza are included, as far as they are
	  • Cost-effectiveness analyses (CEA),
	  • Cost-utility analyses (CUA)
	  • Cost-benefit analysis (CBA) or
	Cost Comparison analyses (CCA) on the basis of clinical studies, observational studies, analyses of secondary data or models.
	
	Ethical, social, legal considerations (ESL)
	All studies are included that contribute towards answering the questions raised here.

Setting[1]	Medical section: All regions Other parts: *Narrow:* Germany *Broad:* Europe, USA, Canada, Australia
Publication language	German or English
Publication type[3]	Full publication

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Exclusion criteria	
***P**articipant* **(patient/proband)**	*Indication:* • Studies relating to monovalent or bivalent LAIV • Studies with LAIV not based on the master donor viruses A/Ann Arbor/6/60 and B/Ann Arbor/1/66 (e.g. LAIV of Russian origins/donor strains A/Leningrad/134/17/57 or B/Leningrad/14/55) • Influenza viruses H5N1 and N7N9 • Influenza in animals *Age:* • Studies that did not include children up to 18 years of age In the ethical/social/legal section, no consideration was given to monocentric studies, i.e. conducted only in one region or a single location.
***I**ntervention* **(intervention/ exposure)[1]**	*Narrow:* Studies without reference to LAIV *Broad:* Studies without reference to influenza vaccines
***C**omparison* **(comparative intervention)**	• Studies that compare various drug-based or non-drug-based interventions without including LAIV as one of the treatment options • Non-analytical single-arm studies without comparison/reference group
***O**utcomes* **(target criteria)**	• Studies that reported on none of the efficacy- or safety-related endpoints defined in the inclusion criteria • Surrogate parameters of clinical efficacy (e.g. elevation of antibody titre after vaccination) In the ethical/social/legal section, no consideration was given to studies that referred to pandemic scenarios or the access of minority groups within the population to influenza vaccinations.
Study type	For the epidemiological section: RCT[4] For all sections: • Non-analytical single-arm studies without comparison/reference group • Studies without effect size calculationsAnimal studies
Setting	*Age:* Studies that included children up to 18 years of age, but that did not report age-stratified analyses for this target population. *Region:* All other countries[5]
Publication language	Other than German or English
Publication type	For the health-economic section: Systematic reviews For all sections: • Non-systematic reviews, commentaries, letters, case reports or series, contributions to discussion or editorial contributions, methodological publications • Conference contributions (abstracts, presentations, poster), for which no full-text

	publications are available • Studies with insufficient information on methodology • Duplicates

[1] For the sections epidemiology, health economics as well as ethical/social/legal considerations: if an insufficient body of evidence for LAIV ("narrow") exists regarding the endpoints defined under target criteria, the inclusion criteria can be expanded to influenza vaccines in general ("broad").
[2] "Randomised study" in this context only refers to studies in which individual study participants have been randomised. Studies in which groups of people, e.g. pupils of a particular school were randomly assigned to interventions (known as cluster-randomised studies) were not taken into consideration for the medical section, but may be included in the epidemiological one.
[3] In addition, HTAs and systematic reviews are captured as full-text versions for subsequent screening for further RCT or meta-analyses of RCT.
[4] These are included in the medical section.
[5] Not in the medical section; here all countries were included.

CBA = *Cost-Benefit Analysis*; CCA = *Cost-Comparison Analysis;* CEA = *Cost-Effectiveness Analysis; CUA* = *Cost-Utility Analysis*; HTA = Health Technology Assessment; RCT = Randomised Controlled Trial

ARI = acute respiratory infection; FFU = fluorescent focus units; ILI = influenza-like infection; LAIV = live-attenuated influenza vaccine; QALY = quality-adjusted life year; SAE = serious adverse event; TIV = trivalent inactivated influenza vaccine, AE = adverse event.