Genetic vaccines (mRNA/DNA) in animal use

Implications for animal health, human health, our combined microbiome and environment

Special considerations for use as “Countermeasures under Public Health Emergency”

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Genetic DNA/RNA Vaccines for Animals/Fish

- 2005, APEX-IHN (Novartis/Elanco) for Atlantic salmon against Infectious Hematopoietic Necrosis Virus (IHNV), British Colombia.
- West Nile Innovator - DNA (Fort Dodge Animal Health/Pfizer) for West Nile virus in condors and horses.
- Oncept (Merial) against dog melanoma.
- In 2017, CLYNAV (Elanco), a polyprotein-encoding DNA vaccine against Salmon Pancreas Disease Virus (SPDV) infection in Atlantic salmon was authorized by the European Medicines Agency (EMA).
- Sequivity (Merck) in swine (2017) – Emergency use in Canada, fully licensed in US (USDA, 2021). “Platform” for making farm-specific injections based on RNA-particle technology.

Collins et al, “DNA Vaccines in Fish and Aquaculture” https://doi.org/10.1016/j.fsi.2018.07.012

Risks to human genome/biome are not properly studied, waived off as “small chance”… claim rapid degradation of DNA plasmids (in mice)…

6. Safety aspects

Some potential risks have been associated with DNA vaccination. With respect to the vaccinated host, these include integration into genome and disruption of biological processes, and potential unwanted immune responses such as auto-immunity or tolerance to the pathogen [175,176]. Limited data is available for fish, but no significant adverse effects on the host have been identified in initial safety testing in humans [177].

The risks to the consumer concerns the potential ingestion of any residual plasmid from food products, containing elements such as human viral promoter regions (such as the CMV promoter) or antibiotic resistance genes that could potentially have harmful consequences if integrating into the consumers' genome or taken up by their gut microflora. However, this risk is considered negligible since the consumer is one step removed from the presentation of vaccine to the vaccinated animal, and at the site of vaccine injection there is a rapid degradation of the plasmid, within 90 min after vaccination in mice [178]. Fast degradation of the plasmid has also been observed in fish [82]. Con-

DNA Plasmids Found in Fish Muscle 320 Days Post Vaccination!

Table 8. Persistence of plasmids in epaxial muscle of rainbow trout collected at different days post-vaccination (dpv) during the field trial.

Trial	Time Point (dpv)	Plasmid Detection		
			pVax1-vhsG-Positive	pVax1-ihnG-Positive
Potency test		90	5 /5	5/5
Field trial		120	1/5	1/5
		160	3/5	3/5
		180	3/5	2/5
		210	2/5	2/5
		230	3/5	3/5
		260	4/5	0/5
		280	0/5	0/5
		320	6/15	6/15

Efficacy of DNA Vaccines in Protecting Rainbow Trout against VHS and IHN under Intensive Farming Conditions

by Andrea Marsella [1,*], Francesco Pascoli [1], Tobia Pretto [1], Alessandra Buratin [1], Lorena Biasini [1], Miriam Abbadi [1], Luana Cortinovis [1], Paola Berto [1], Amedeo Manfrin [1], Marco Vanelli [2], Simona Perulli [2], Jesper S. Rasmussen [3], Dagoberto Sepúlveda [3], Niccolò Vendramin [3], Niels Lorenzen [3] and Anna Toffan [1]

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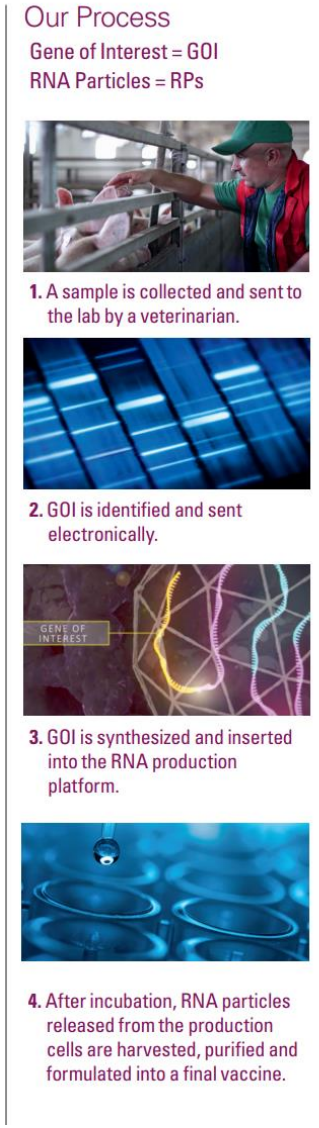
Merck Sequivity RNA “platform” for pigs

- USDA approved for swine influenza in December 2021
- Synthetic (not-natural) RNA in nanoparticle
- No information available on the chemical composition of nanoparticle, nor its toxicities by itself:
  - No biodistribution studies available
  - No genotoxicity studies available
  - No carcinogenicity studies available
  - No published safety studies available in peer reviewed literature
- Collect and centralize genomic surveillance data from farms:
  - How is the data used? Who can access it? For what purposes?



MERCK Animal Health

SEQUIVITY®

USDA Label, Safety Summary (p.18)

Adverse Events Summary 21 days

VeDDRA Code	Total Animals	Percent of All Animals
No adverse events	525	70.20%
Anorexia	55	7.40%
Death	24	3.20%
Lameness	20	2.70%
Loss of Condition	12	1.60%
Diarrhea	11	1.50%
Unthrifty	7	0.90%
Anaphylaxis^	3	0.40%
Central Nervous System Disorder*	3	0.40%
Lethargy	3	0.40%
Respiratory Tract Infection*	3	0.40%
Arthritis	2	0.30%
Meningitis	2	0.30%
Musculoskeletal Disorder*	2	0.30%
Trauma*	2	0.30%
Abdominal Caviry Hernia	1	0.10%
Abscess*	1	0.10%

*Not otherwise specified

^Related to IVP

USDA Approval Date	December 13, 2021

30%!

https://www.aphis.usda.gov/wcm/connect/