Vaccines: a key tool to tackle antimicrobial resistance (AMR)

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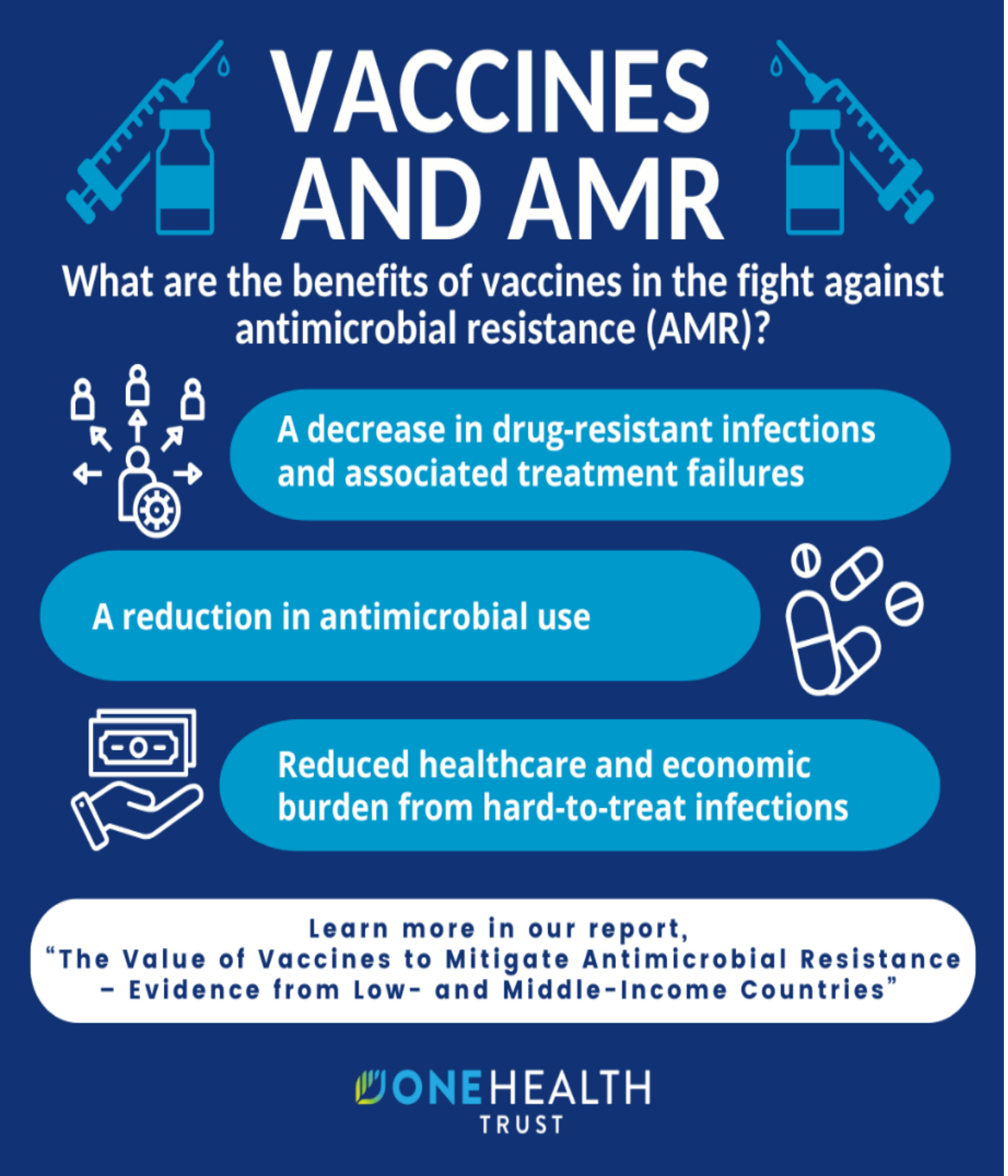


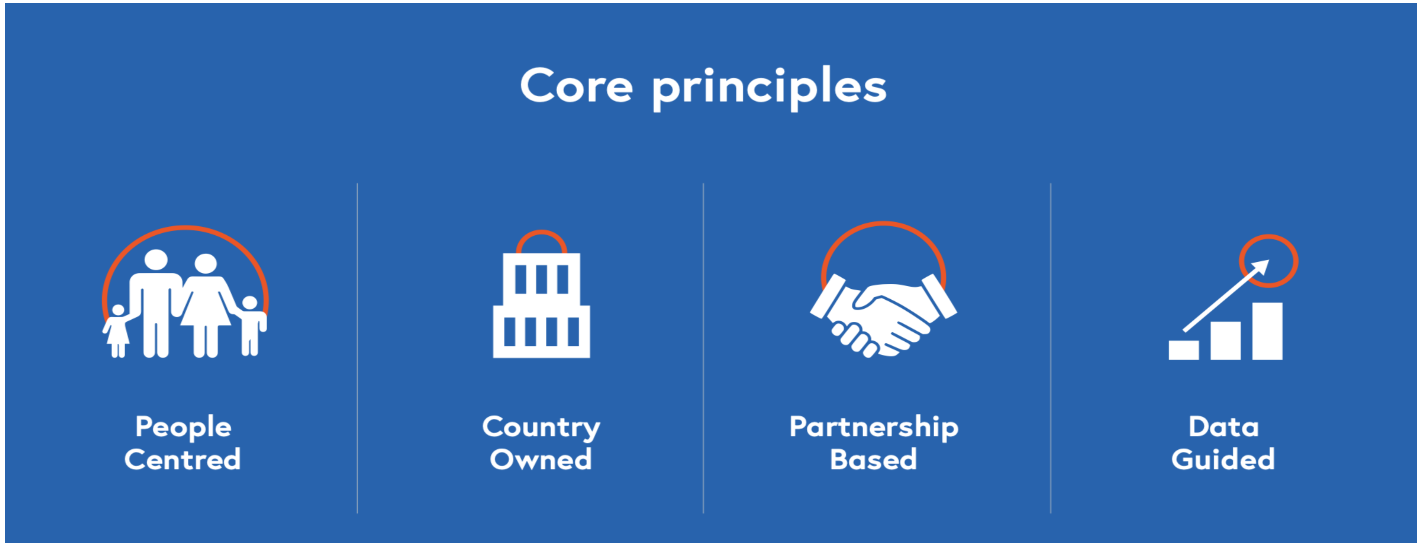
Vaccination is a global health & development success story

Immunization agenda 2030: WHO released an action framework that describes a vision for vaccines to contribute ***<u>fully, sustainably and equitably</u>*** to the prevention and control of AMR

- Immunization is the <u>backbone of the primary health care system</u>: saving millions of lives every year!
- The COVID-19 pandemic has reminded the world of the power of vaccines to fight disease, save lives.
- An essential tool for promoting the health and sustainability of aquaculture

IA 2030: A Global Strategy ”To Leave No One Behind”

WHO have an AMR-focused action framework that summarizes ways to use vaccines both to reduce antibiotic usage & to prevent the further emergence of AMR



People Centred	Country Owned	Partnership Based	Data Guided
Responding to populations needs- addressing barrier to access	Driving progress from the bottom up- approach to ensure vision & goals align with country needs	Aligning efforts to maximize impact by different partners	Promoting evidence-based decision making-to track progress & improve performance

Source: IA 2030- WHO, Geneva 2020

Strategic vision for use of Vaccines in AMR

1. Expanding use of licensed vaccines to maximize impact on AMR

- Increase coverage of vaccines
- Update guidelines to strength immunization programs to support vaccination

2. Developing new vaccines that contribute to prevention and control of AMR

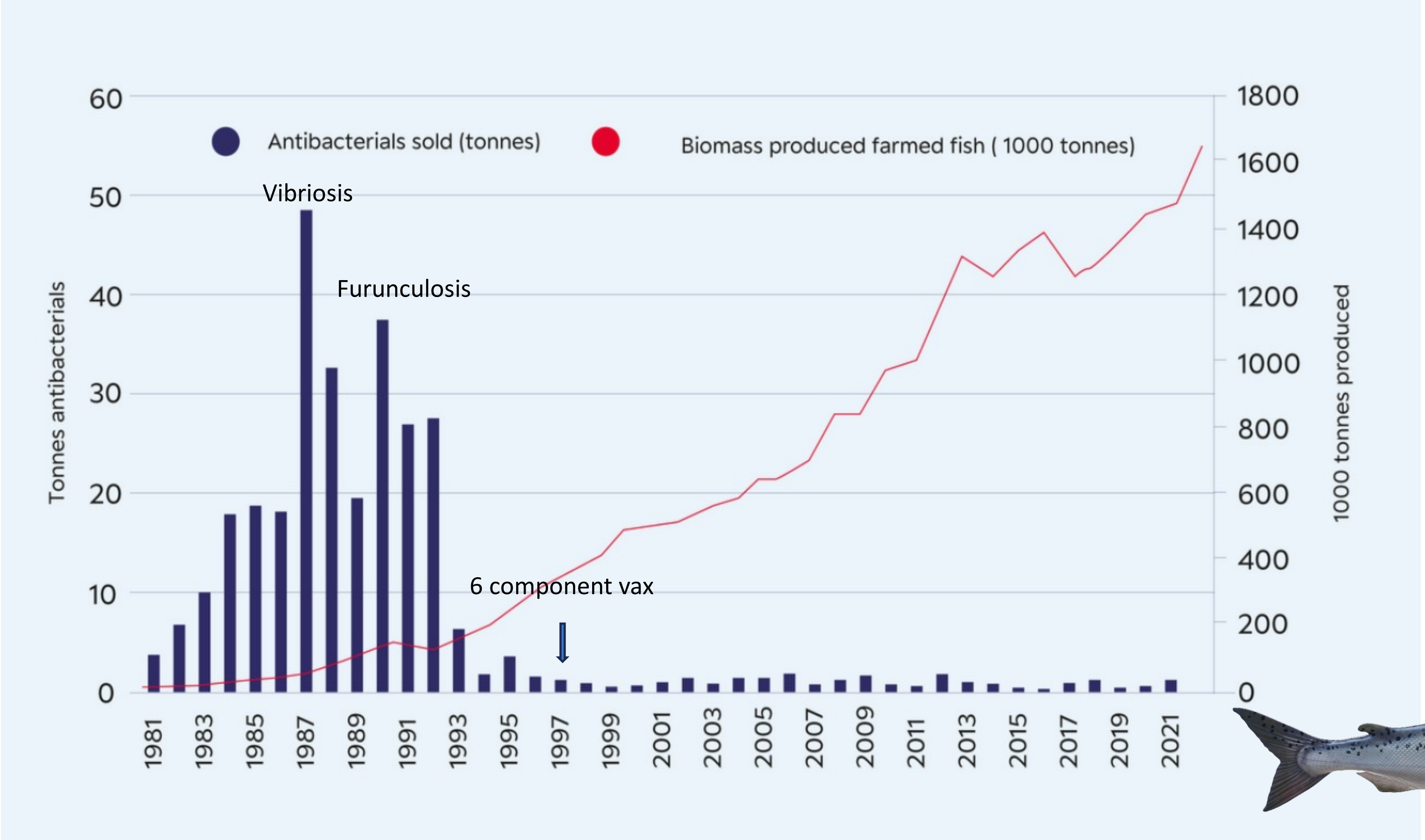
- Bridge funding gap for R&D of new potential vaccines
- Develop regulatory & policy guidelines to accelerate approval and use of new vaccines

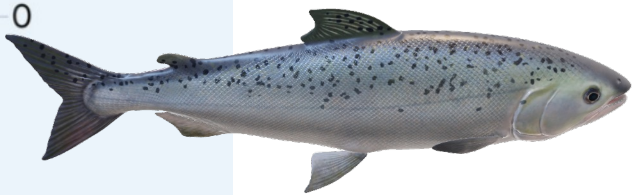
3. Expanding and sharing knowledge of vaccine impact on AMR

- Improve methodologies & analysis of relevant data to assess vaccine impact on AMR, including antimicrobial use.
- Improve awareness & understanding through effective training and education.

Source: IA 2030: Leveraging Vaccines to Reduce Antibiotic Use and Prevent Antimicrobial Resistance (2021)

Fish vaccination success story: antibiotic usage in relation to Norwegian salmon production



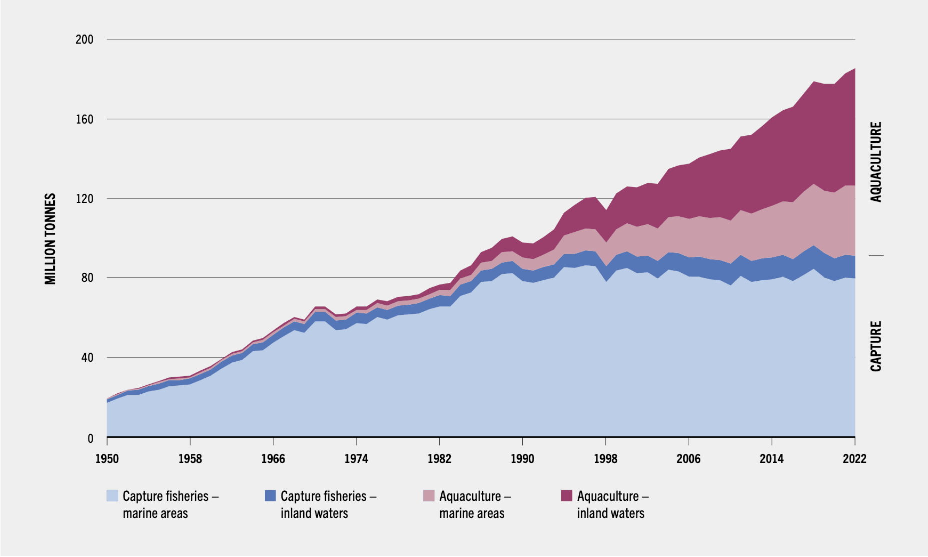


Source: Norwegian Seafood council

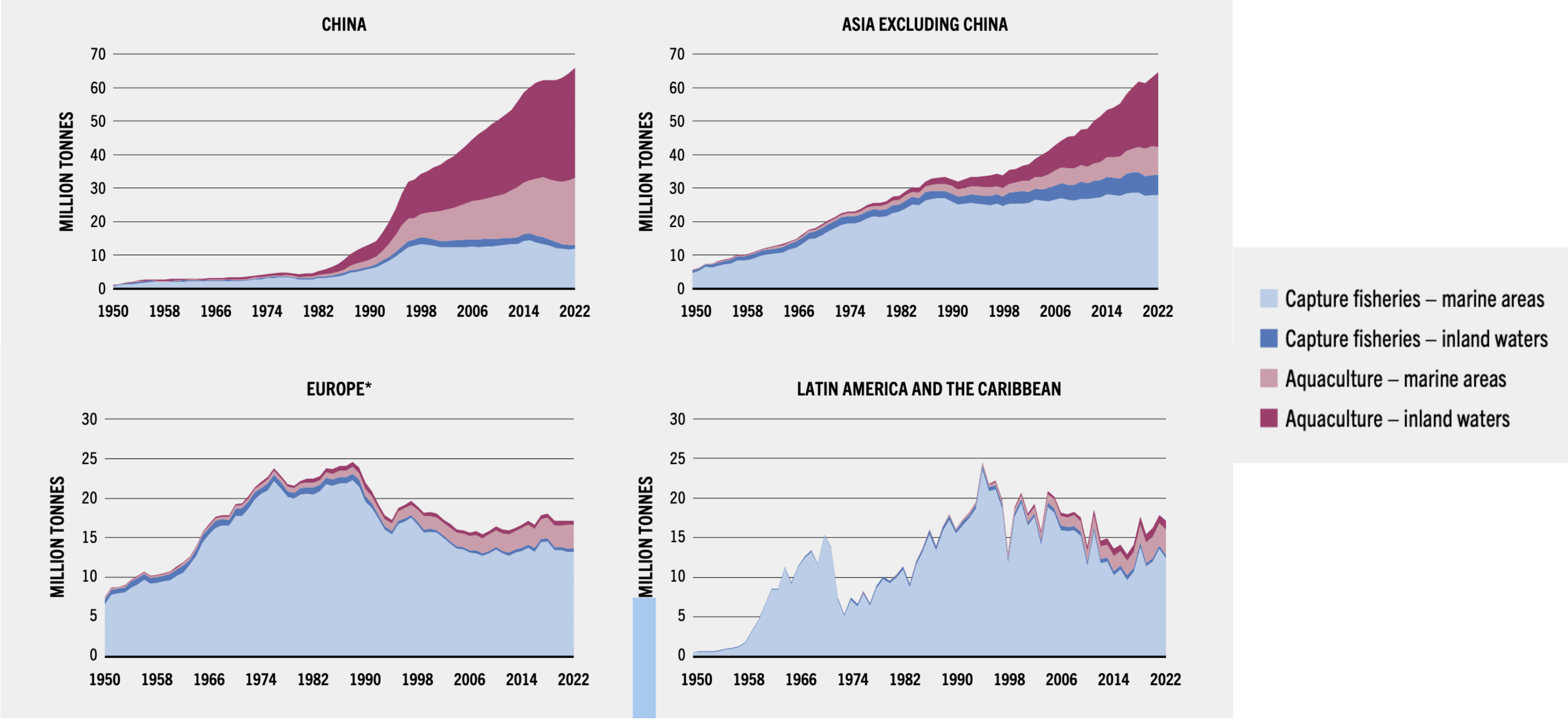
SOFIA, 2024: Aquaculture production of aquatic animals surpassing capture fisheries for the first time

- ✓ Global production- 223.2 MT (FAO report 2024-new record high)
- ✓ Global aquaculture production- 130.9 MT (51% Aquatic animals).
- ✓ Record production of aquatic foods underlines the sector’s potential in tackling food insecurity and malnutrition

FIGURE 1 WORLD FISHERIES AND AQUACULTURE PRODUCTION OF AQUATIC ANIMALS



World Fisheries and Aquaculture production of aquatic animals, 1950-2022



- Aquatic animal production by region: Asia (70 percent)
- Main producers (globally): China (36 percent), India (8 percent), Indonesia (7 percent), Viet Nam (5 percent).

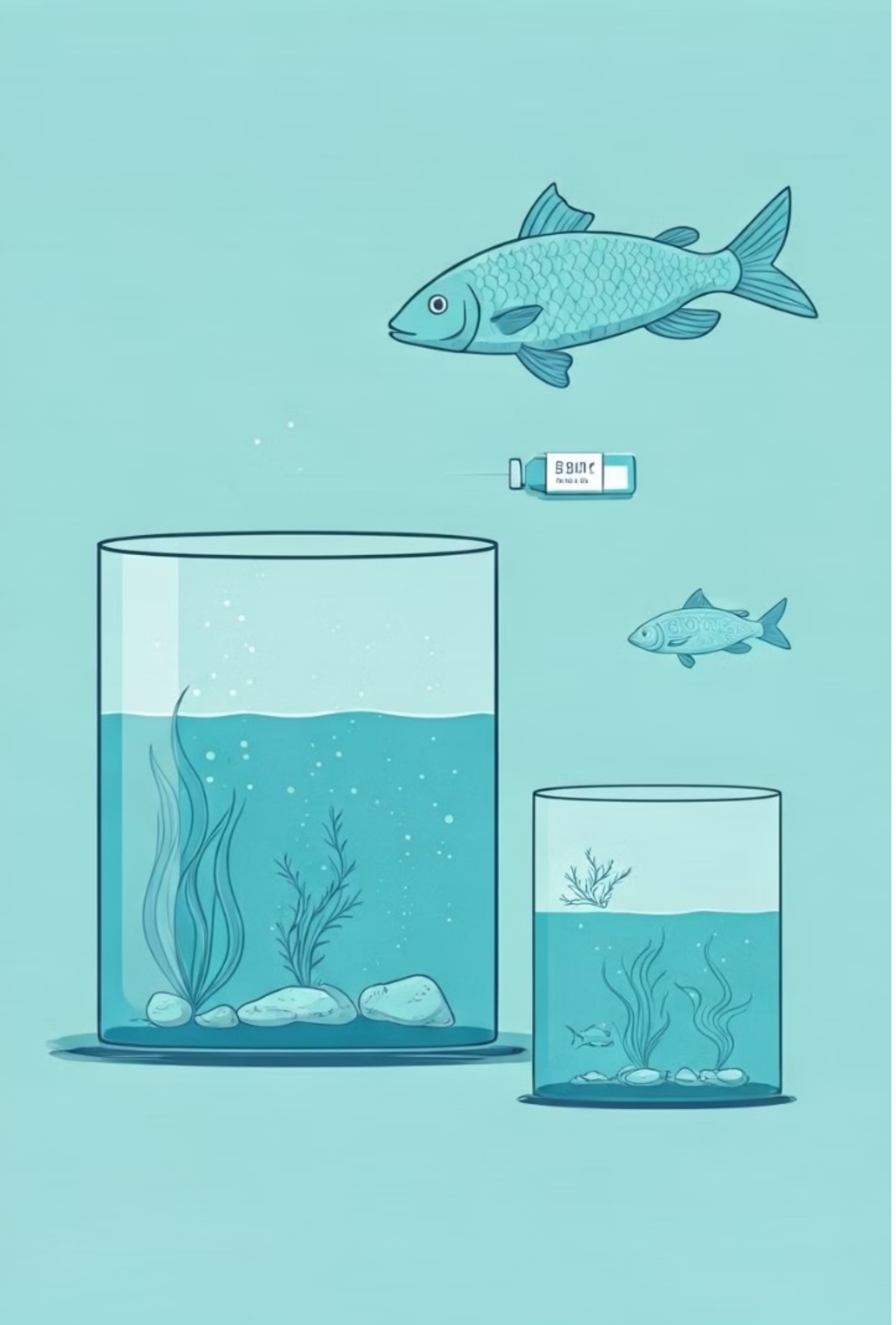
Source: FAO 2024-Fishstat

Overview of licensed fish vaccines according to the region

Region	Licensed vaccines against different pathogenic organisms		Major fish host
USA	Virus	IPNV	Salmonids
	Bacteria	*Yersinia ruckeri; Vibrio* spp.; *Aeromonas salmonicida; Renibacterium salmoninarum; F. columnare; Pasteurella piscicida*	Salmonids, grouper, sea bass, sea bream, cod, halibut
Canada	Virus	IHNV; IPNV; ISAV;	Salmonids
	Bacteria	*Y. ruckeri; Vibrio* spp.; *A. salmonicida; R. salmoninarum*	Salmonids, grouper, sea bass, sea bream, cod, halibut
Latin America	Virus	IPNV; ISAV; SAV	Salmonids, sea bass, sea bream, turbot
	Bacteria	*R. salmoninarum; Streptococcus* spp.; *Piscirickettsia salmonis*	Salmonids, yellow tail, rainbow trout, sea bass, sea bream, tilapia
Europe	Virus	IPNV; ISAV; SVCV	Salmonids, carp
	Bacteria	*Y. ruckeri; Vibrio* spp.; *A. salmonicida; P. piscicida; Lactococcus garviae; Moritella viscosa; Tenacibaculum maritimum*	Salmonids, turbot, Rainbow trout, grouper, sea bass, seabream
Australia	Bacteria	*Vibrio* spp.; *A. salmonicida;*	Salmonids, grouper, sea bass, sea bream
Asia (except SE Asia)	Virus	KHV	Carp
	Bacteria	*Vibrio* spp.; *P. piscicida; Streptococcus* spp.	Salmonids, tilapia, yellow tail, rainbow trout, ayu, sea bass, sea bream
SE Asia			
Singapore	Virus	ISKNV	Asian seabass, grouper, Japanese yellowtail
Indonesia, Thailand	Bacteria	*Streptococcus* spp.	Tilapia
Vietnam	Bacteria	*Edwarsiella ictaluri; Aeromonas* spp.	Striped catfish

Abbreviation IPNV (Infectious pancreatic necrosis virus); IHNV (Infectious hematopoietic necrosis virus); ISAV (Infectious salmon anemia virus); SAV (Salmonid alphavirus); SVCV (Spring viremia of carp virus); KHV (Koi herpesvirus); ISKNV (Infectious spleen and kidney necrosis).

- 1938: 1st vaccine- Trout, Orally-Salmonicida
- 1976: 1st commercial vaccine registered in USA
- Currently: >30 vaccines in global market



Limitation of existing vaccines

Variable efficacy

Vaccine efficacy is influenced by many factors: pathogens (genetic variation), vaccine factors (type, adjuvant, dose & administration) and host factors (age, genetics, nutritional & immune status, gut microbiota etc.,)

Limited availability

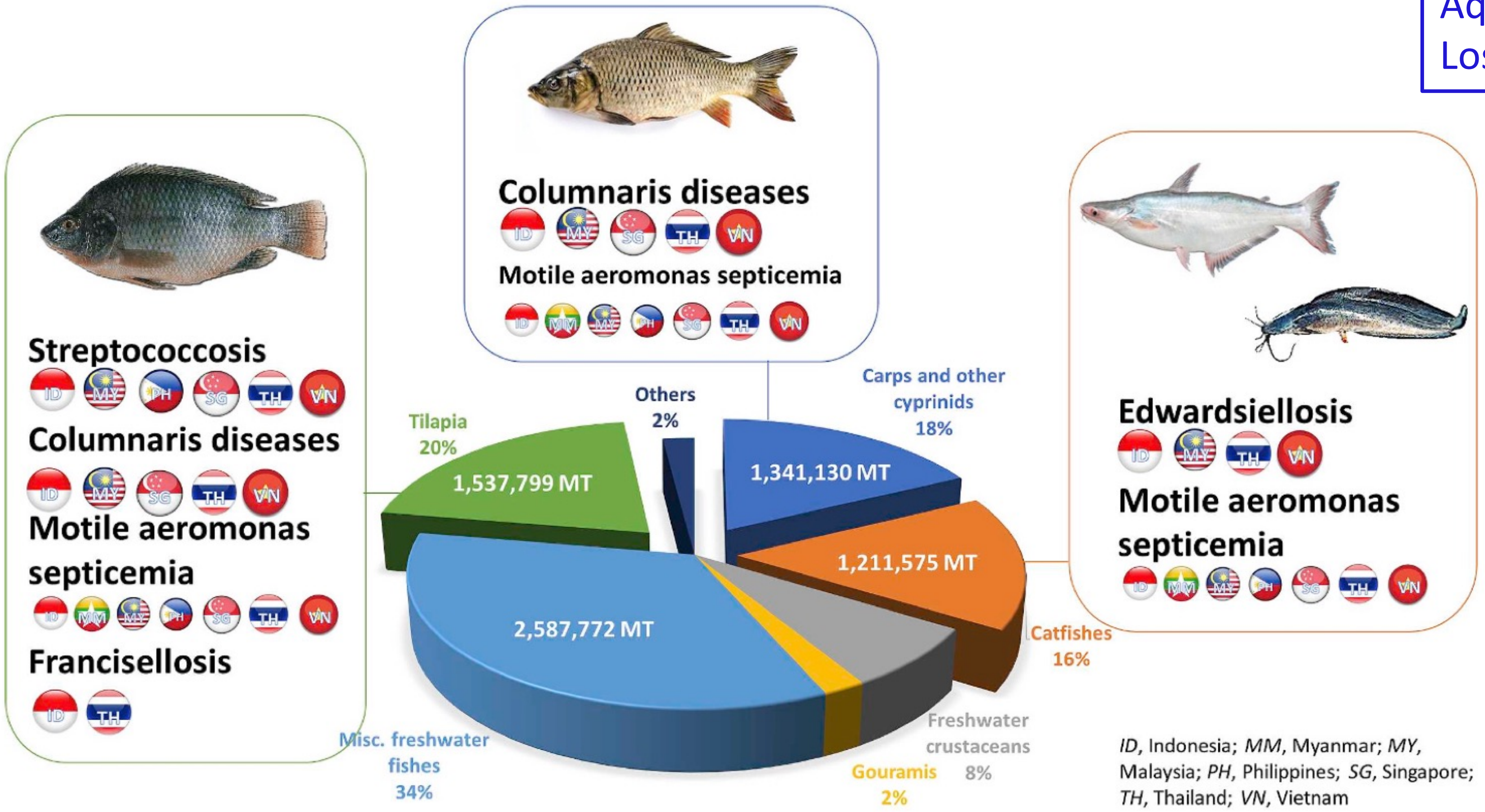
Vaccines are not readily available for all fish diseases, and some vaccines may be costly or difficult to administer.

Emerging pathogens

New diseases are constantly evolving, and current vaccines may not be effective against all emerging pathogens.

Disease outbreak- a serious threat to sustainable production

Aquaculture sector- est. $100B (NPV)
Losses due to diseases: ~21% ($10 B)



- Several serotypes
- Limited serotype profiling

Source: Kayansamruaj et al., 2020. Fish Shellfish Immunol. 103: 73-87

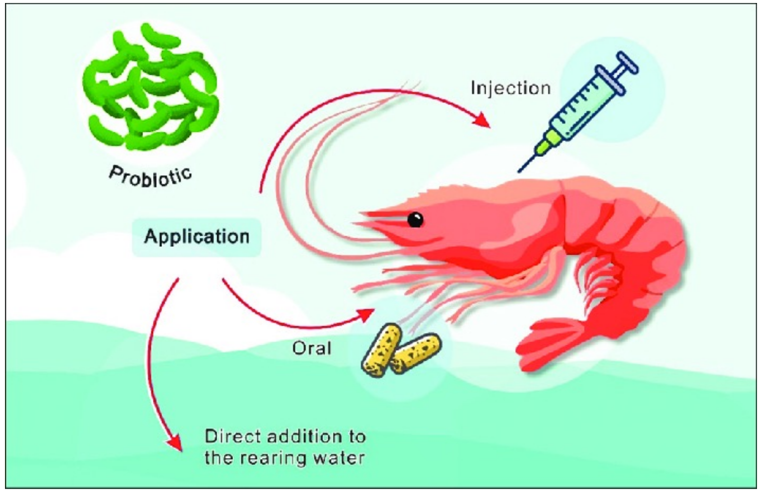
Edwardsiella ictalurid: threatening pathogen to freshwater aquaculture

Picture credit: Dr. T.E Schwedler

- Causes devastating losses in the US and SEA countries since 1999.
- Affects all age group, with fingerlings and juvenile most vulnerable (50-90%)
- AMR resistant strains leads to increased Rx cost
- Increasing susceptibility in novel species including Nile tilapia.
- Increased genetic diversity/serotypes from distinct geographical and host origins. Serotype profiling is limited in SEA.
- Only ONE vaccine available - neutralization of pathogen extracellularly (Ab responses).
- Intracellular pathogen needs stronger CMI.
- Vaccine design should be driven by pathogenicity and molecular epidemiological information of particular country.

Aquatic invertebrates

- Crustacean fisheries have experienced billions of dollars in economic losses.
- Vibriosis and white spot syndrome virus (WSSV)
- Increase in drug-resistant pathogens- V. harveyi strains with multiple resistance to streptomycin, erythromycin and cotrimoxazole causing mass mortalities.
- To date, no effective measures are available to prevent or control disease outbreaks
- Simple immune system- innate functions (physical barriers & cellular and humoral components-hemocytes).
- Existence of an alternative quasi-specific immune responses (simplified immune memory)- can be primed via immunomodulatory feeds, RNA interference technologies etc.,



Amiin et al., Vet. World (2023), 16(3): 638

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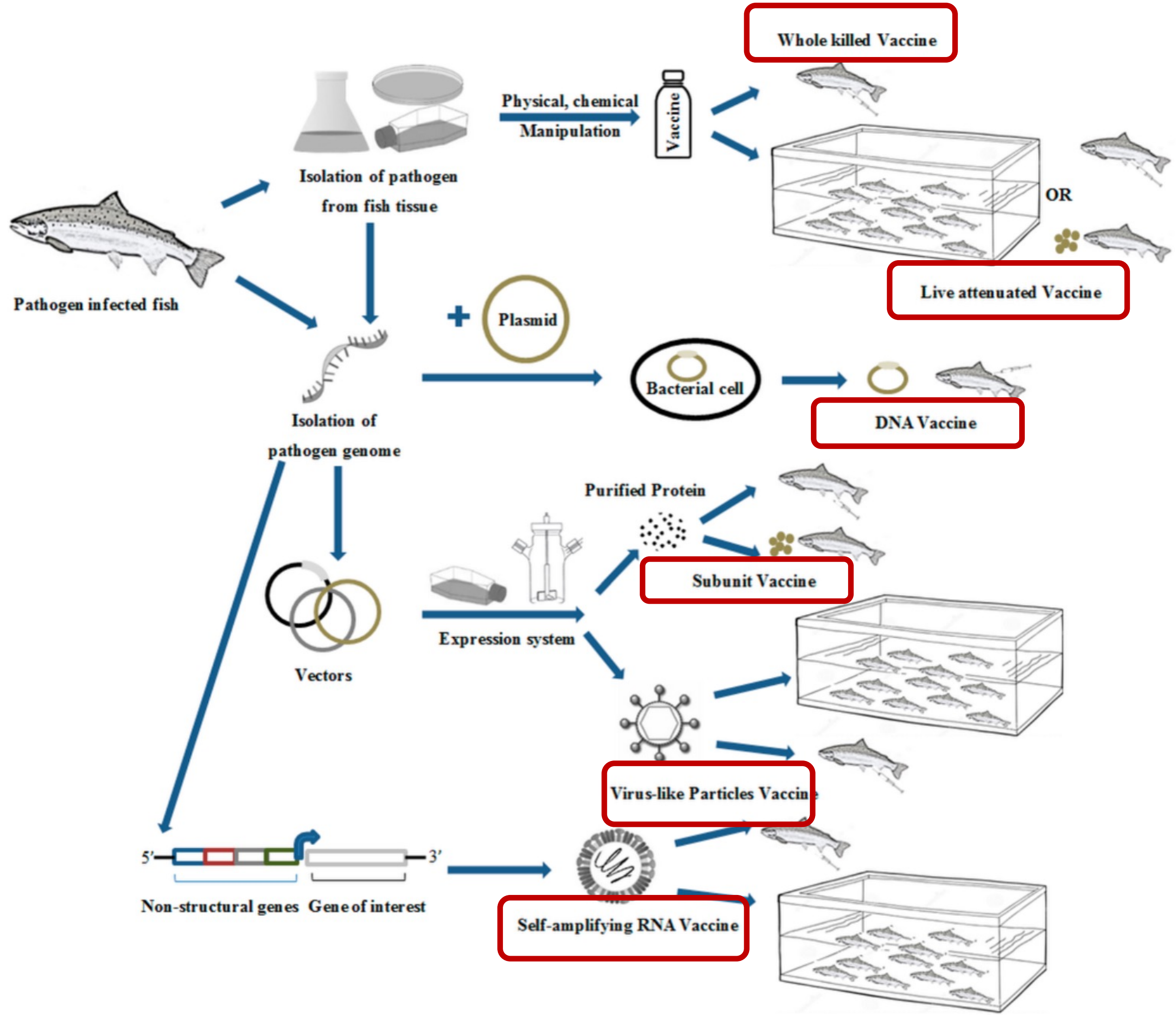
Limitations with vaccine development in Asia

- Quite alarming to see very few licensed vaccines are available
- SEA not a lucrative market for big Pharma companies
  - low value species, high cost of vaccines
  - High level of fragmentation and weak distribution infrastructures & services.
  - Different/slow vaccine registration policies.
  - Lack of user friendly delivery systems/skilled team
- Different licensed vaccines in each country
- Many vaccines in developmental stage but limited licensed vaccine available in the market.
- Lack of education and communications

Vaccine development strategies

- ✓ Autogenous vaccines to tackle novel and emerging diseases
- ✓ In-depth understanding of fish immunity help develop better delivery systems (Immersion/Oral)
- ✓ Priorities important disease with higher impact (with high risk of AMR)
- ✓ Pathogen categorization & sharing among SEA countries to support the development of broad-spectrum vaccine
- ✓ Financial support to develop new vaccines and R&D technologies to develop vaccines from scratch & clinical trials
- ✓ Increase uptake- support vaccine initiatives in the region to educate farmers
- ✓ Explore alternatives

Conventional & Modern Biotechnological Approaches to fish vaccine development



Source: Ma et al., *Microorganisms* (2019), 7: 569

Novel & innovative vaccine Technologies

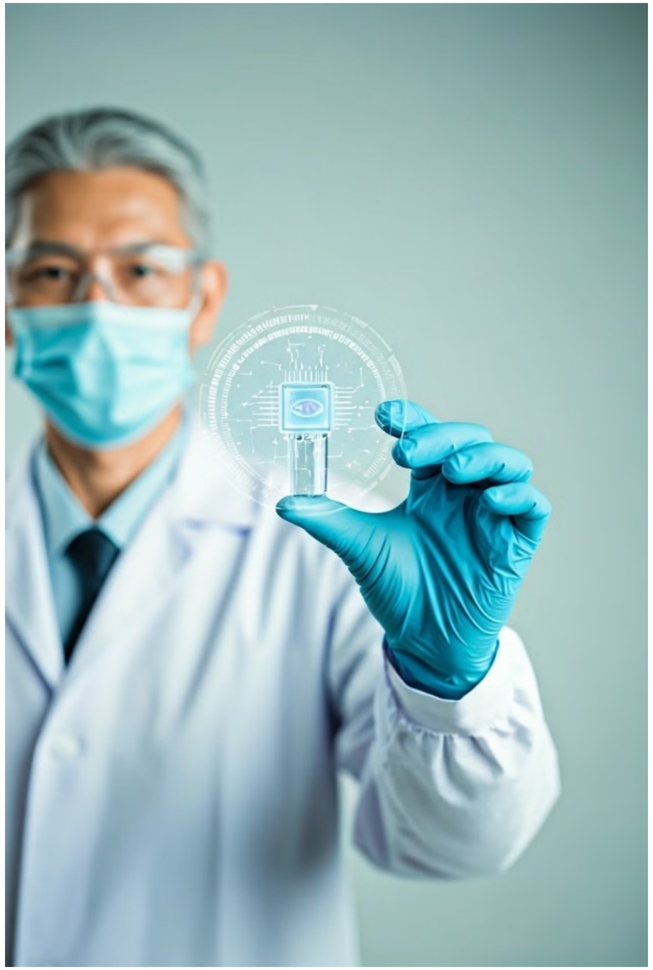
Alternative novel vaccines (using multi-omics technologies)	mRNA vaccines	High immunogenicity & low cost
	Vector vaccines	antigen precision & delivery, high safety
	Synthetic peptides-Epitope based vaccines	Highly immunogenic & precision

Oral vaccines	Plant-based vaccines	Cost effective, adjuvant effect, efficient antigen expression, post-translational modifications
	Encapsulation- Polymer & Bioencapsulation	Cost effective, adjuvant effect, biocompatibility

Reverse vaccinology	Bioinformatics tools & computational models to identify common antigens	Cross-protective against multiple antigens

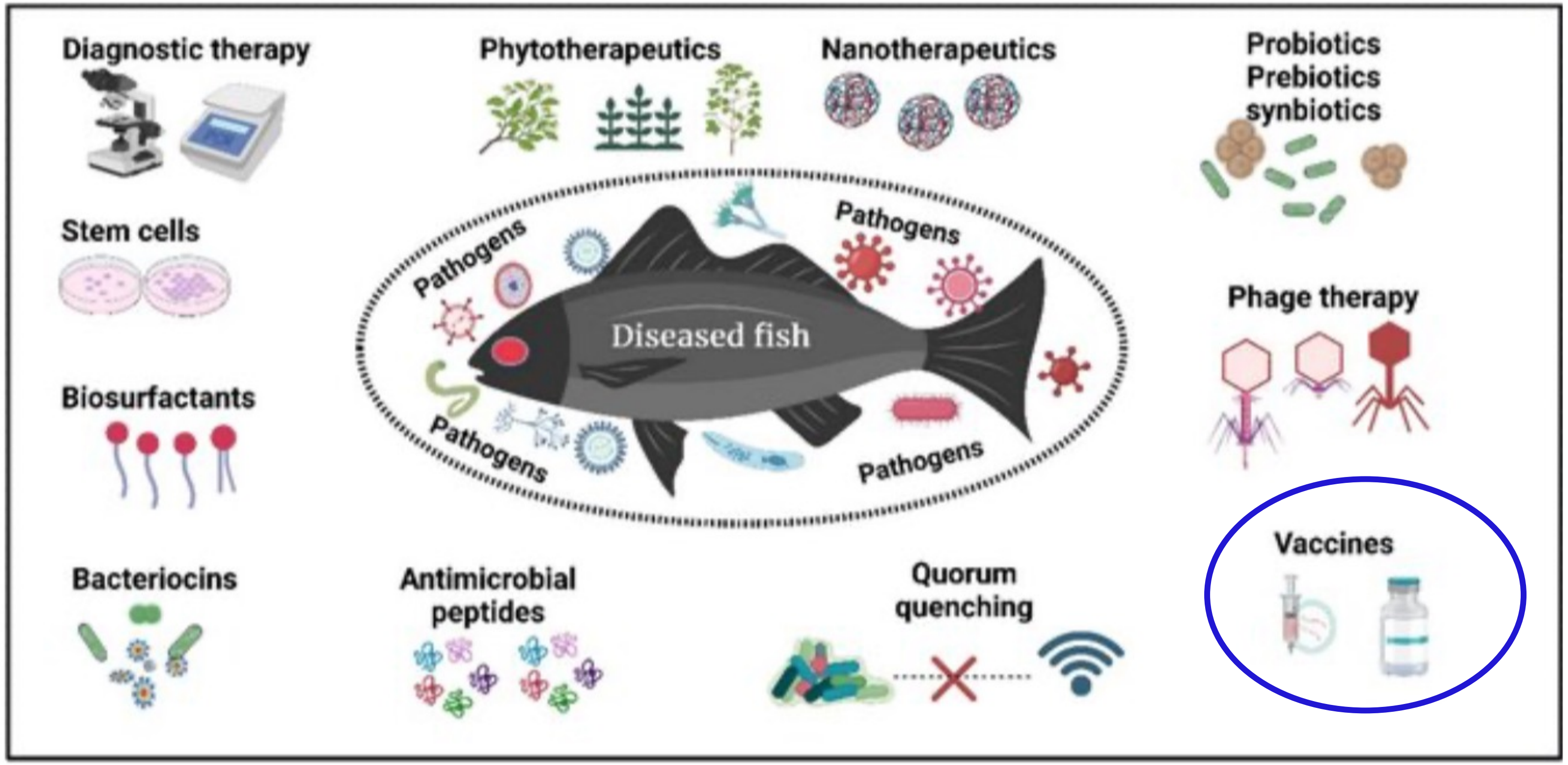
Adjuvants	Fish cytokines, Nanoparticles	Increased efficacy, mucosal delivery

Parasites	DNA vaccines and encapsulation technique	Complexity, need extensive R&D

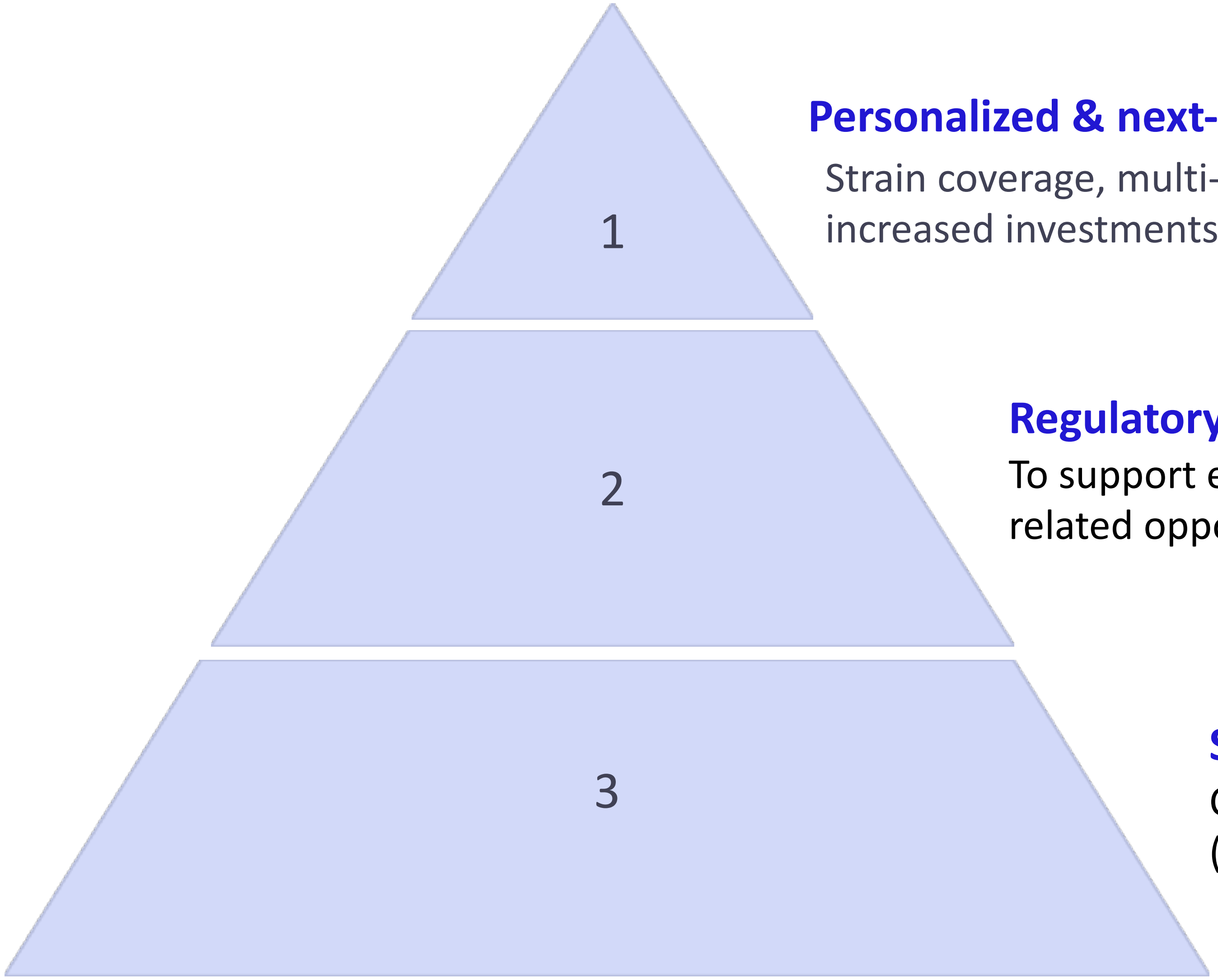


Source: Tammas et al., Vaccines (2024), 12: 732

Alternative therapies for treating fish diseases



Future Directions: Personalized Vaccines & Novel Approaches



Personalized & next-generation vaccines

Strain coverage, multi-valent vaccines, efficient delivery systems, increased investments

Regulatory and policy frameworks

To support efficient decision-making & to maximize vaccine-related opportunities and impact.

Surveillance and data collection

Communication & education, quick diagnostic analysis (disease diagnosis & Ab sensitivity tests)

Successful Vaccine Deployment

Reduced Mortality

Vaccines have significantly reduced mortality rates in fish populations, leading to higher production and improved profitability.

Increased Production

Vaccination programs have resulted in increased fish production, contributing to a more sustainable and reliable food supply.

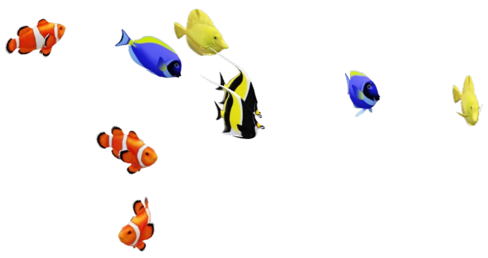
Improved Sustainability

Vaccines have reduced the reliance on antibiotics, promoting sustainable aquaculture practices and minimizing the risk of AMR.

Accelerate vaccines.
Stop AMR.

International Vaccine Institute

Thank you



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