CTCVAC

The Answer Beyond Animal Health Care



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Development for challenging

of New generation vaccines pathogen: P. Salmonis

R&D Division, CTCVAC Director, D.V.M., Ph.D. JUNG, Ho kyoung



A BRIEF INTRODUCTION



It's been a long journey.

ICN to PMC: 39 hours 51 minutes Flight time 31H41M, Layover time 8H10M

- S. 0



A BRIEF INTRODUCTION

I'm from South Korea.

The Opposite side from Chile, Northern hemisphere Five words, represent Korea:

- Seoul
- Korean cuisine,
- **K-POP**
- Technology(SAMSUNG, LG, HUNDAI)
- Beautiful natural environment





NATURAL ENVIRONMEN



K-POP





SOUTH KOREA

CAPITAL CITY

POPULATION

* SEOUL

FLAG

LOCATION

COREAN CUISINE

A BRIEF INTRODUCTION



l'm a researcher.

Developing vaccine for animal and aqua Over 20 years experience Vaccine development and application



I work for CTCVAC in Korea.

- Company name: CTCVAC co., Ltd.
- Year of Foundation: April 2019
- No. of Employees: 42 Employees
- Business Area

Animal biological products (Research, Manufacture and Sales)

• Major Research

Animal biological products(especially, Vaccine) and other Preventive strategies for Animal infectious disease GMP-certified animal vaccine manufacturing facility. Vaccine Research and Development Center Expanded R&D network





For sale : 14 Products (as of Jan 2024)



CSF Marker + Erysipelas
 live vaccine



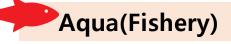


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- ND, IB, ND-IB (Killed)
- FAdV(type 4), FAdV II(type 4,8)
- YBBEN(LPAI-IB-ND-EDS), YBB(LPAI-IB), YAP(LPAI-FAdV-aMPV)







- DAJAVA killed vaccine (Scutica *Miamiensis avidus* + *Tenacibaculum martimum*)
- Bac-DAJAVA killed vacccine
 (Streptococcus Ic, Ia, Edward)



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HIPRA STARTVAC (Mastitis vaccine)



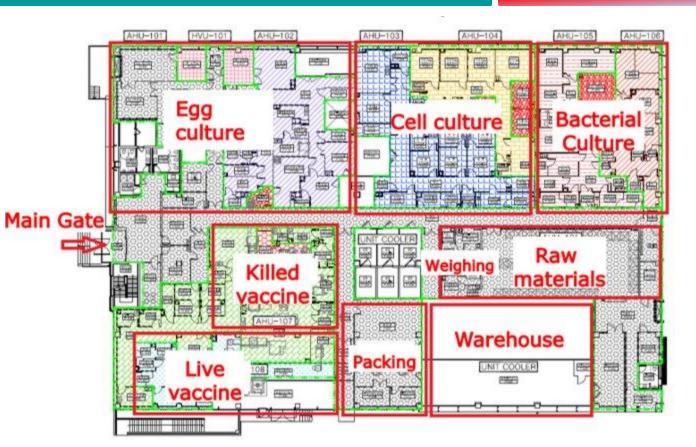




• Purpose

Manufacture of Veterinary Vaccine (Swine, Poultry, Bovine, Fishery and Companion animal)

- GMP certification
 Nov. 2016, EU/US GMP Guidelines
 applied
- Total building Floor area
 5,958 m² (3 floors)



Production

Antigen bulk: Virus from egg embryo, virus from cell-culture, Bacterial culture, Plasmid DNA, Purified recombinant protein Finished Products: Live vaccine, Killed vaccine, Recombinant vaccine, DNA vaccine





- Main Facilities and Purification equipment for Aquatic
- Bacteria and Scutica cultures
 Fermenter : 50L, 100L, 600L, 1,000L
 Purification equipment :FPLC, UF/DF
 - High-density culture of strain such as *Streptococcus* spp., Edward's,

Vibriospp. and Tenacibaculum maritimum.

Scutica(*Miamiensis avidus*) culture by fermenter system.

Virus culture

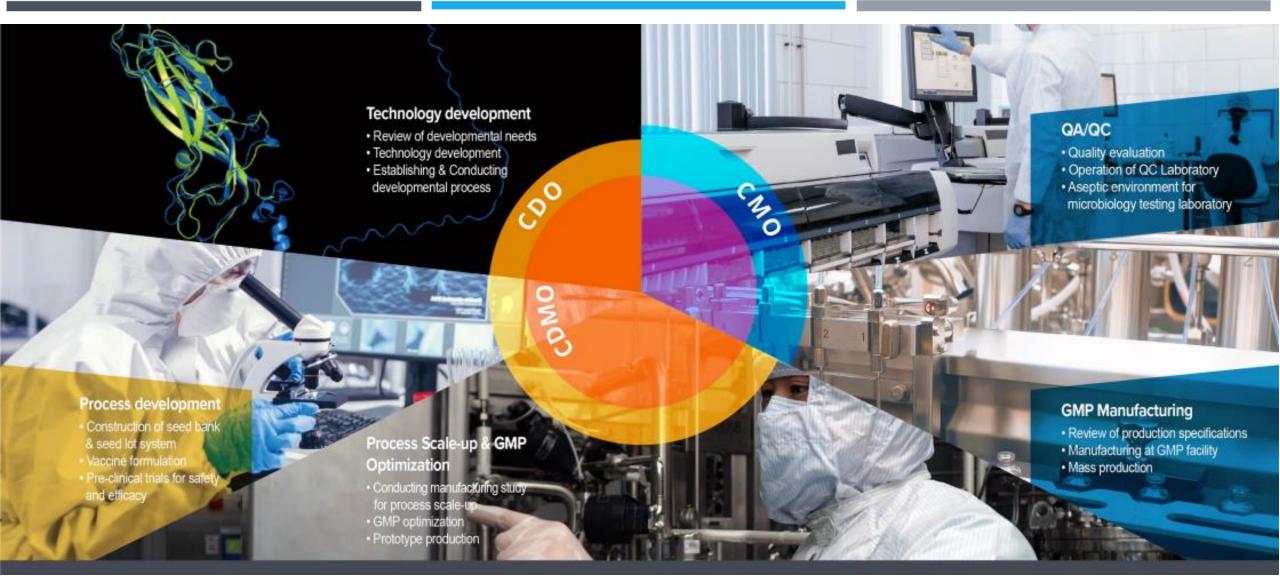
Roller bottle culture system for viral strain 100bottle/unit x 10unit = 200L High titer culture technology for VHSV

Freeze dryer for live vaccine production



Fermenter

Expansion of business scope_CMO/CDMO/CDO







South Korea is the 4th largest consumer of seafood in the world

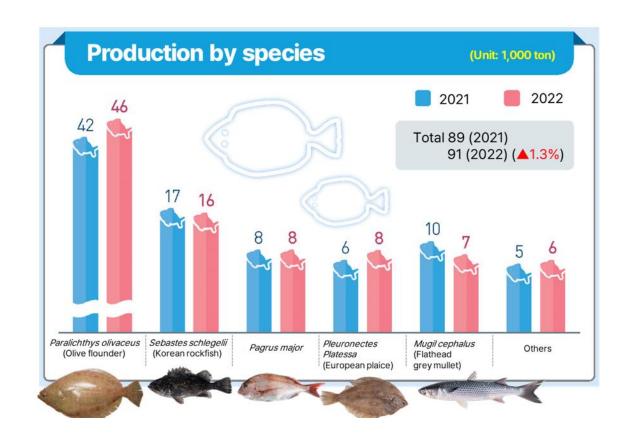


* estimates based on per capita food supply, not adjusted for food waste Source: UN Food and Agriculture Organization



statista 🗹

The Olive flounder (Paralichthys olivaceus) has ranked at the top of production among cultured finfish in S. Korea for more than 10 years.





Vaccine Sales: 9 mill. USD in 2008 → 31 mill. USD in 2018 (+ 244%) (6 mill. doses) (63 mill. doses) (+ 963%)

10years

- Six vaccine manufacturers in Korea
- Number of shots until market
 - 1 shot 35%
 - 2 shots 52%
 - 3 shots 13%



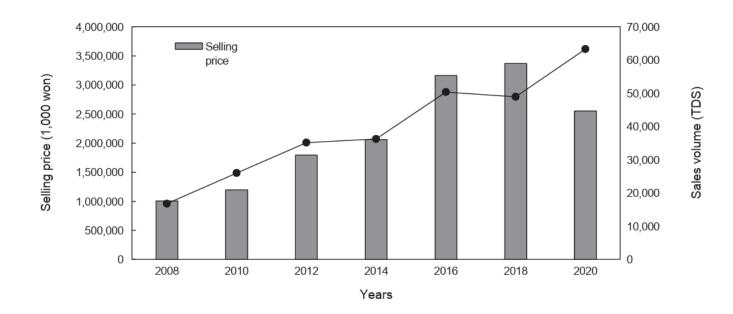


Fig. 2. Fish vaccine annual sales volume (Thousand doses, TDS) and selling price (Thousand won) in Korea from 2008 to 2020.

Ref.: Hyun-Ja Han, Tae-Ho Kim, Soo-Jin Kim, Myoung-Sug Kim, Mi-Young Cho, Hye Sung CHOI. Current status and future directions of fish vaccines in Korea. Korean J Fish Aquat Sci 54(4),369-376,2021



Vaccinated fish in Korea

Olive flounder



Starry flounder



Rock seabream



Table 1. Licensed product fish vaccines in Korea

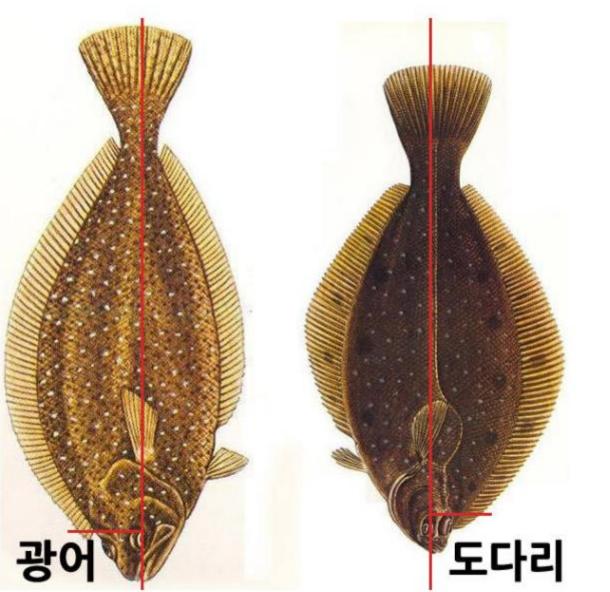
Vaccine	Target pathogen (No. of pathogen)	Fish species	No. of product	Year of approval	Use
	Edwardsiella tarda (1)	Olive flounder	2	2003, 2005	Immersior
	Streptococcus iniae (1)	Olive flounder	6	2006, 2007	Immersior
	S. iniae+Streptococcus parauberis (2)	Olive flounder	5	2009, 2010, 2012	Injectable
	S. iniae+S. parauberis+E. tarda (3)	Olive flounder	5	2010	Injectable
Bacteria	Listonella anguillarum+ <i>S. iniae</i> + <i>S. parauberis+E. tarda</i> (4)	Olive flounder	1	2010	Injectable
	L.anguillarum+ Tenacibaculum maritimun+ S. iniae+S. parauberis+E. tarda (5)	Olive flounder	1	2012	Injectable
	Lactococcus garviae+ <i>V. harveyi+S. iniae</i> + <i>S. parauberis+E. tarda</i> (5)	Olive flounder	1	2015	Injectable
	L.anguillarum+V. harveyi+S. iniae+ S. parauberis+E. tarda (5)	Olive flounder	1	2018	Injectable
	V. harveyi+S. iniae+S. parauberis+E. tarda (4)	Olive flounder	1	2010	Injectable
	<i>S. parauberis</i> la+lb/c (2)	Starry flounder	1	2019	Injectable
Parasite	<i>Miamiensis avidus</i> type I+ <i>Miamiensis avidus</i> type II (2)	Olive flounder	1	2019	Injectable
Parasite+ bacteria	<i>M. avidus</i> type I+ <i>M. avidus</i> type II+ <i>T. maritimum</i> (3)	Olive flounder	1	2019	Injectable
Virus	Viral hemorrhagic septicemia virus (VHSV) (1)	Olive flounder	1	2019	Injectable
	Red seabream iridovirus (Ehime-1/GF) (1)	Red seabream, yellow tail rock seabream	· 1	2004	Injectable

Ref.: Hyun-Ja Han, Tae-Ho Kim, Soo-Jin Kim, Myoung-Sug Kim, Mi-Young Cho, Hye Sung CHOI. Current status and future directions of fish vaccines in Korea. Korean J Fish Aquat Sci 54(4),369-376,2021

Olive flounder

: Paralichthyidae

Differentiation by Eye Position: Left



Starry flounder :Pleuronectidae

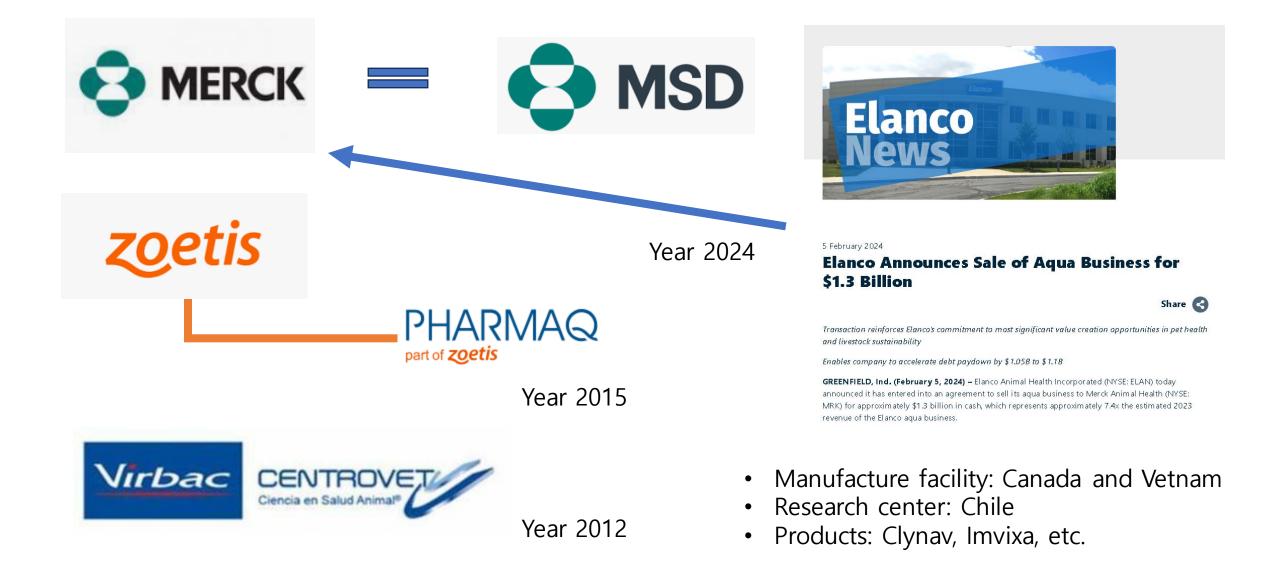
Right



- 1. Change in your surrounding
- 2. Health report in Chile
- 3. Pathogens and vaccine
- 4. Considerations for vaccine development
- 5. New generation vaccine for *Piscirickettsia salmonis* (SRS)

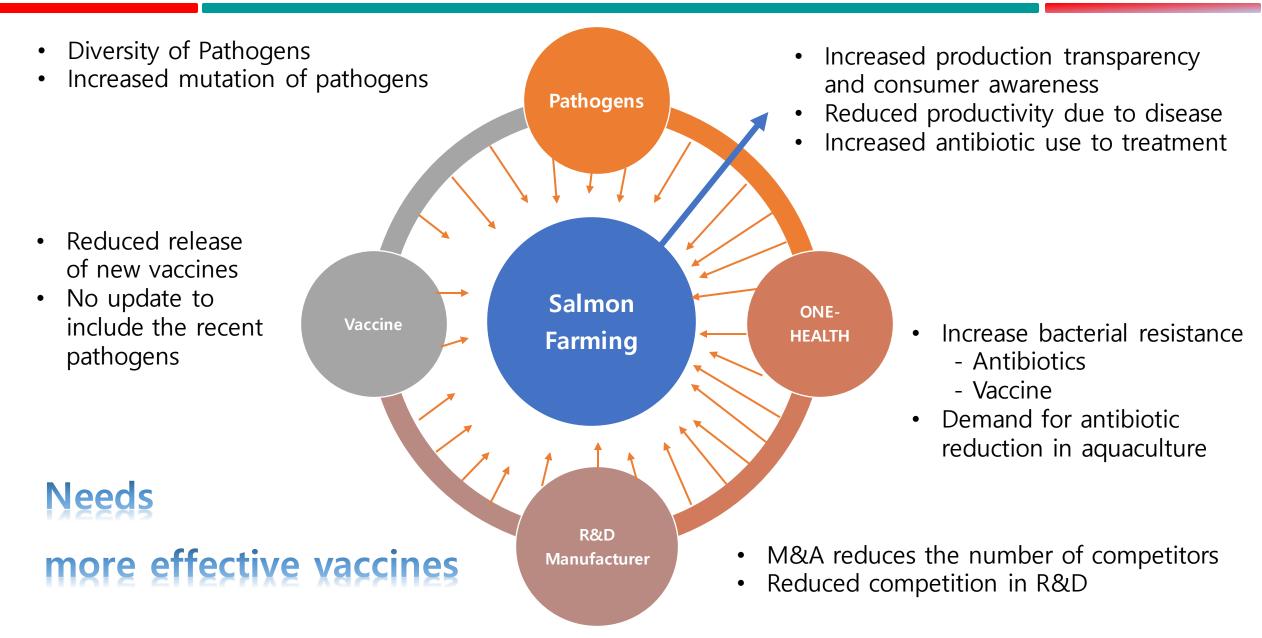
CHANGE IN YOUR SURROUNDING





CHANGE IN YOUR SURROUNDING







During the first half of 2023

Monthly mortality in Chilean salmon:

- Max. 1.24% (in May),
- Min. 0.65% (in June)
- Average 0.86%

In the case of **Atlantic salmon**, the most important cause of mortality reported was infectious (26.9%)

- 52.2% as Piscirickettsiosis (SRS)
- 32.9% as Tenacibaculosis

In the case of Rainbow trout; infectious cause (24.6%)

IPN was the most important with 68.8%, followed by Piscirickettsiosis with 17.7%.

Salmonexpert Bolsa Laboral Mitos y Verdades Descargas Nosotros



Informe sanitario: buenas noticias con menor mortalidad para el salmón chileno



Chile: La mortalidad en la salmonicultura chilena obtuvo un valor promedio mensual de 0,86%, cifra que es menor 0,4%. Sernapesca también reveló la mortandad por empresa en su informe sanitario.

Jonathan Garcés Periodista y responsable web

PUBLICADO 12.01.2024 - 05:00

PATHOGENS AND VACCINE

Bacteria

- *Piscirickettsia salmonis* (SRS)
- Aeromonas salmonicida (furunculosis)
- Vibrio ordalii (vibriosis)
- Tenacibaculum spp. (ulceration)

Virus

- Infectious Salmon Anemia Virus (ISAV)
- Infectious Pancreatic Necrosis Virus (IPNV)

PHARMAQ Norvax[®] Minova 6 ERM, RELERA® Slice® Integrated Sea Lice ALPHA JECT[®] 5-1 Injectable vaccines part of zoetis & Oral Boos It is an inactivated, multivalent vaccine against furunculosis, classical vibriosis, coldwater vibriosis, wound manageme disease and infectious pancreatic necrosis (IPN) for intraperitoneal injection in Atlantic salmon. 3. Composición 15-09-2020 3. Composición Cada dosis (0,1 mL) contiene: Composición por dosis REGISTRO SAG N°2497-BP Virus de la Necrosis Pancreática Infecciosa COMPOSICIÓN SERVICIO AGRÍCOLA Y GANADERO serotipo Sp (IPNV), Cepa AL V103 0.15 - 0.25 AU Sustancias activas: Cada dosis de vacuna (0.1 mL) contiene 108.5 - 108.8 TCIDe ettsia salmonis, Cepa PS 2i Cada dosis contiene Piscirickettsia salmonis, Cepa AL10005 0,075 - 0,11 mg proteína Aeromonas salmonicida subsp. salmonicida, Cepa AL 2017 1.5 - 2.0x 108 células Vibrio ordalii, Cepa AL 510 0,5 - 1,0 x 108 células Virus de la Necrosis Pancreática Infecciosa Vibrio ordalii, Cepa AL 510 0.5 - 1.0x 108 células 107.0 - 107.5 TCIDe ALPHA JECT® micro 4-2 epa Sp221Ala, Serotipo Sp Aeromonas salmonicida subespecie 107,0 - 107,5 TCIDer Cepa Sp221Ala, Serotipo Sp Virus de la Necrosis Pancreática Infecciosa, Serotipo Sp., 0,15 - 0,25 AU salmonicida, Cepa AL 2017 1,0 - 2,0 x 108 células Cepa AL V103 107,0 - 107,5 TCIDe Virus de la Anemia Infecciosa del Salmon Virus de la Anemia Infecciosa del Salmón, Cepa AL V301 0.4 - 0.45 HE-U Cepa Sp221Thr, Serotipo Sp 1,0 - 7,5 x 107 TCID50 (ISAV), Cepa AL V301 Excipientes c.s.p. 0.05 mL 107/9 - 107/5 UFC Vibrio ordali/, Cepa VD44-03 irus de la Necrosis Pancreática Infecciosa Advuvante: Parafina líquida epa Sp221Thr, Serotipo Sp 10^{7,0} - 10^{7,5} TCID₅₀ -Inactivante: Formaldehído 107.0 - 107.3 UFC 5,4 - 8,1 µg IPNV, ISAV, Vibrio ordalii, Aeromonas salmonicida, 4 combined vaccine in Chile IPNV, ISAV, Vibrio ordalii, A. salmonicida, SRS 5 combined vaccine in Chile xcipientes c.s.p. 5,4 - 8,1 µg 0,1 mL ISA recomb., SRS, IPNV, V. ordalii, A. IPNV vaccine ALPHA JECT micro 4 3. DEKLARASJON AV VIRKESTOFFER OG HJELPESTOFFER Aeromonas salmonicida - Listonella (Vibrio) anguillarum - Vibrio salmonicida salmonicida 7 combined vaccine Bacterin 1 dose (0,1 ml) vaksine inneholder: COMPOSICIÓN ALPHA JECT[®] micro Injectable vaccines Description Formaldehydinaktiverte kulturer av: TOPPOTE A furunculosis, vibriosis and cold water vibriosis vaccine containing: formalin inactivated Cada dosis de vacuna (6 mg) contiene ALPHA JECT[®] 6-2 Injectable vaccines Aeromonas salmonicida subsp. salmonicida $RPS^1 > 80$ (Ph. Eur.) cultures of Aeromonas salmonicida subsp. salmonicida, Listonella (Vibrio) anguillarum $RPS^1 \ge 90$ (Ph. Eur.) Vibrio salmonicida serotypes O1 and O2 and Vibrio salmonicida. Piscirickettsia salmonis, Cepa PS 20 10^{8,0} - 10^{8,5} TCIDe Listonella anguillarum serotype O1 $RPS^1 \ge 75$ (Ph. Eur.) Vibrio salmonicida V. anguillarum , A. salmonicida, SRS 4 combined vaccine in Canada Listonella anguillarum serotype O2a $RPS^1 \ge 75$ (Ph. Eur.) Virbac CENTROVET $RPS^1 \ge 60$ Moritella viscosa Excipientes c.s.p. Infeksiøs pankreasnekrosevirus serotype Sp. 0.2 AU 6 mg

Risk

MSD Active ingredients MSD Animal Salmon pancreas disease virus (SPDV) strain F93-125, ≥ 75 % RPP1 **Health Hub**

ERM & IPN

Infectious pancreatic necrosis virus (IPNV), ≥ 1.5 ELISA units²

Aeromonas salmonicida subsp. salmonicida, ≥ 80 % RPS603

² Antigenic mass measured in the final product

¹ RPP: relative percentage protection in a laboratory test in Atlantic salmon

SPDV, IPNV, A. salmonicida combined vaccine

IPN, Frunculosis, Vibriosis, winter sores,

PD and Sea Lice

³ RPS: relative percentage survival at 60 % control mortality in a laboratory test in Atlantic salmon

IHNV DNA vaccine in use in Canada





Aquavac® IPN Oral

It is a recombinant, oral vaccine against Infectious Pancreatic Necrosis virus (IPNv) in Atlantic salmon (Salmo salar). Allows for protection of fry in the hatchery at a very early stage in the production cycle

Norvax[®] Compact PD

It is an inactivated virus vaccine against Salmonid Alphavirus (SAV) for intraperitoneal injection in Atlantic salmon (Salmo salar)

A. salmonicida, Vibrio salmonicida, V. anguillarum, Winter ulcer, IPNV 8 combined vaccine in Norway and U.K.

SRSV oral vaccine

PATHOGENS AND VACCINE



When do we consider developing a new vaccine?

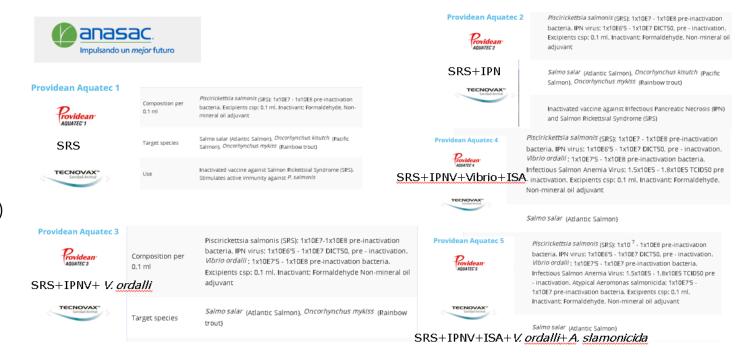
Outbreaks(or predictions) of new diseases Mutated pathogens emerge – in(or less)effective to existing vaccines

Bacteria

- Piscirickettsia salmonis (SRS)
- Aeromonas salmonicida (furunculosis)
- Vibrio ordalii (vibriosis)
- *Tenacibaculum* spp. (ulceration)

Virus

- Infectious Salmon Anemia Virus (ISAV)
- Infectious Pancreatic Necrosis Virus (IPNV)



CONSIDERATIONS FOR VACCINE DEVELOPMENT



R&D sector

- Selection of effective antigens
- Proliferation yield of antigens
- Vaccination protocol and programs

Manufacturing

- Mass Production Process
- Purification tools
- Achieving low production costs

Targeted vaccine efficacy • RPS in the LAB?

• RPS in the Filed?

Number of shots

Fields

- Efficacy and safety
- The needs to use vaccines
- Forecasting vaccination demand and sales



Our Goals

- Developing a vaccine that can **drastically reduce antibiotic use**
- Development of a vaccine with longer immunity (than existing vaccines)

Our Challenge

T 1. Development of a **Non-Bacterin Vaccine** containing the concentrated antigen obtained from *P. salmonis*

T 2. Development of a DNA Vaccine containing the antigenic gene of *P*. *salmonis*

T 3. Development of SRS Live Vaccine using R-MET technology Scheduled

NEW GENERATION VACCINE AGAINST SRS



Fishfarmingexpert About us Contact Jobs & FFE Newsletter Calendar

T 1. Development of a Non-Bacterin Vaccine containing the concentrated antigen obtained from *P. salmonis*

- Prototype developed at a university in Chile ٠
- The vaccine strain was isolated from salmon in Chile •
- Non-Bacterial antigens produced through a special process •
- Secure high purity of antigen by adding purification process ٠
- Evaluation was conducted at a Chilean research institute • using salmon farmed in Chile.
- Antigen concentration is optimized for Chilean aquaculture ٠ environment.



The best prototype of the vaccine provided an 88.5% protection and a mortality 5-6 days later than the bacterins available in the market. Photo: File Salmonexpert

New prototypes of SRS vaccine developed

Scientists in Chile have developed candidates for prototypes of a vaccine against Piscirickettsia salmonis, commonly known as SRS.

Francisco Soto

PUBLISHED Wednesday 23. January 2019 - 12:20 LAST UPDATED Wednesday 23. January 2019 - 12:34

It is the latest achievement of Dr Alejandro Yáñez and colleagues at the Austral University of Chile (UACh), who have over the years developed culture media and antigens for diagnostic tests for SRS

The disease is a particular problem in Chile, where the lack of a vaccine has led farmers to use far more antibiotics than in other salmon producing countries.

Yáñez told Fish Farming Expert's Chilean sister site, Salmonexpert, that he expects in the near future to be able to generate prototypes of a medium-scale vaccine for SRS, using candidates that in tests for intraperitoneal infection have shown excellent protection (measured by RPS90 - see panel, right), and with results much higher than those obtained from commercial vaccines based on bacterins.

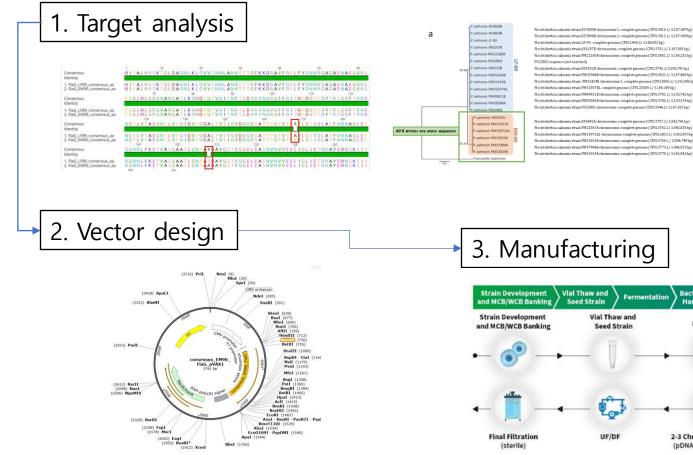
What is RPS 90?

RPS 90 is a comparative index that compares the mortality of the vaccinated fish with the controls when 90% of the controls

NEW GENERATION VACCINE AGAINST SRS

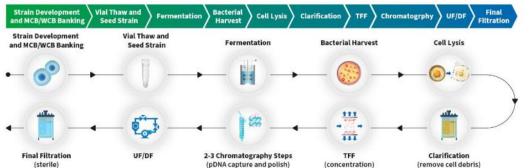


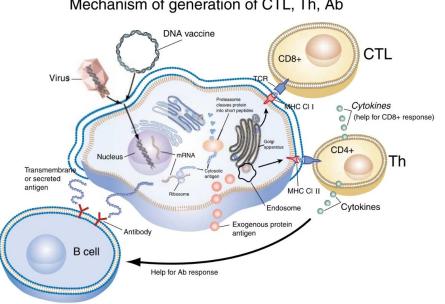
Development of a **DNA Vaccine** containing T 2. the antigenic gene of *P. salmonis*



BbsI (1760)

3. Manufacturing





Liu MA. DNA vaccines: a review. J Intern Med. 2003 Apr;253(4):402-10.

Mechanism of generation of CTL, Th, Ab

NEW GENERATION VACCINE AGAINST SRS



Death

Growth retardation (DNA repair process)

Growth normally

Hydrodynamic

FLUORESCENCE

SCATTERED LIGHT

Labeled

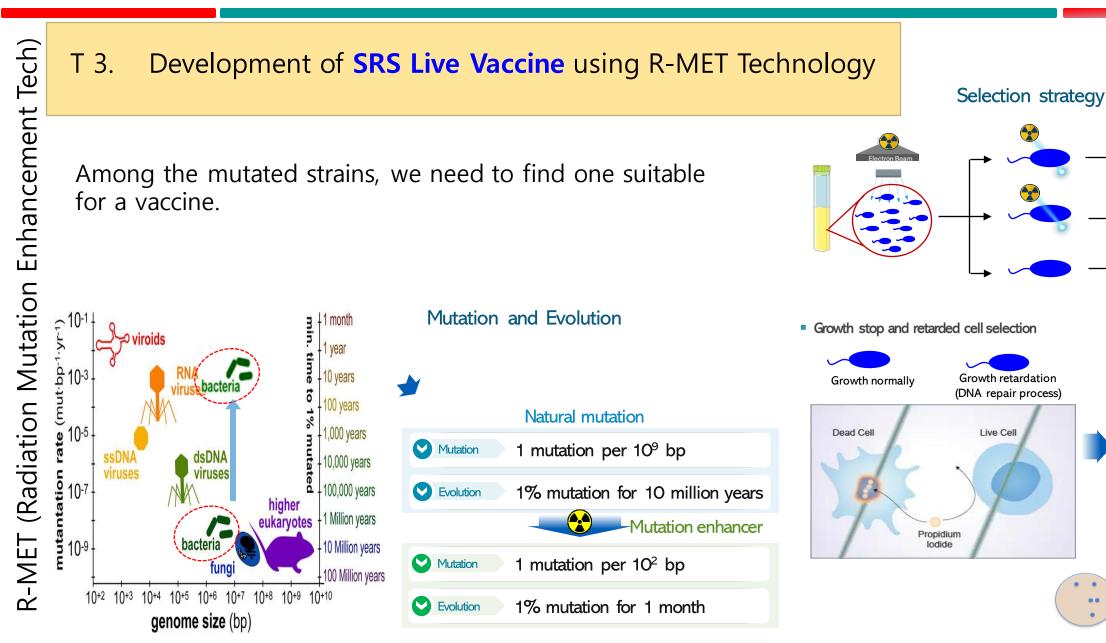
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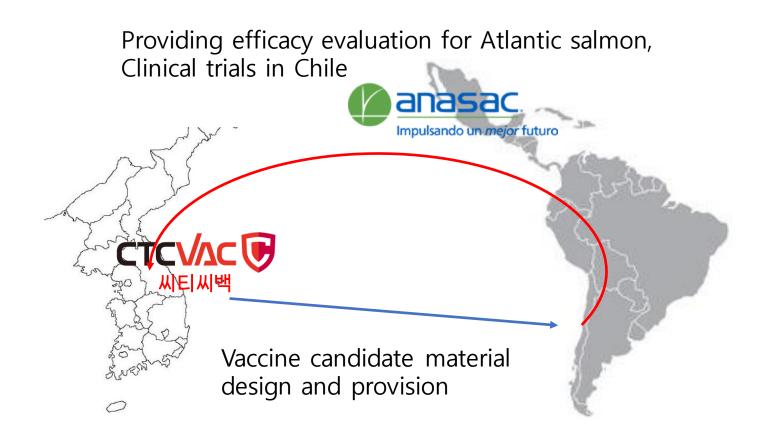


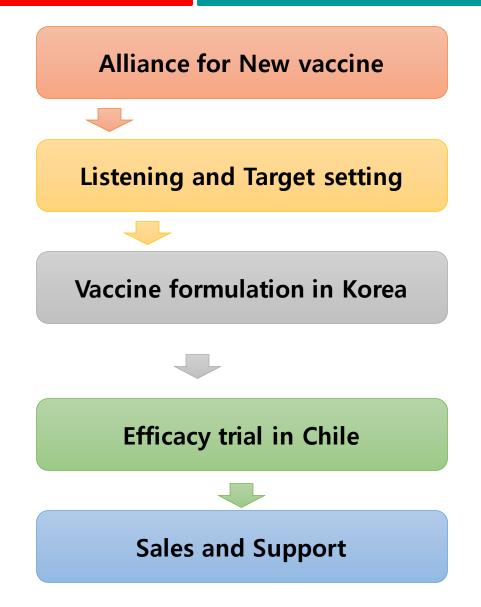


What kind of NEW VACCINES Do You Need? For the prosperity of the Chilean aquaculture industry!



Meeting with Chilean Anasac officials regarding salmon vac. (At the 2022 Eurotier exhibition in Hannover, Germany, Nov. 16, 2022)





• Organizing the Salmon Vaccine Development Alliance

- Distinguishing roles in development, evaluation, registration, and sales
- Listening to needs from the salmon farming field
- Analyzing pathogens from recent target disease cases
- Include antigens based on the recent pathogens
- Antigen combinations for reasonable vaccine program construction
- Developing in multiple formulation: DNA, Recombinant protein, Live attenuated antigen
- Customized **efficacy evaluation in Chilean salmon** farms
- Prioritizing immune sustainability and safety
- Responsible sales and technical support from our Chilean partners

