

# Preparing Europe for the Next Viral Outbreak

*ISTC/IRKUTSK conference*

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MARSEILLE FRANCE

# Necessity to create international infrastructures to allow horizontal spreading of knowledge

- to produce efficient diagnostic protocols for infectious diseases
- to facilitate antiviral drug development

# EVA

# European Virus

# Archives

FP7 Infrastructure project (2009-2012)

**Jean-Louis ROMETTE**  
Professor  
Project coordinator  
AFMB, CNRS/University of  
Marseille  
France

# Rationale to create EVA

## A critical issue

- A parcelar 40 year-old organization
  - James Porterfield & Ernest Gould (Oxford),
  - Jean-Pierre Digoutte (CRORA),
  - Robert Shope (Yale-Center for Biodefense & Emerging Infectious Diseases),
  - Christopher Clegg (National Collection of Pathogenic Viruses at Porton Down)...
- Scarcity of the resource
  - Poor quality of existing collections in Europe
  - No viral stocks available
  - ATCC ceased the supply of viral strains outside of USA, since «9/11»

## A strategic objective

- A key tool for industrial and scientific developments
  - Virological studies
  - Design of new diagnostic tools
  - Design of new vaccines and antiviral compounds
  - Production of derived molecules for scientific and medical researches (antibodies, recombinant proteins...)
- A priority to face new & emerging diseases and biodefence

## EU contribution to EVA

■ IRD	998 622 €
■ VLA	643 941 €
■ BNI	647 000 €
■ UKB	545 040 €
■ NCPV	846 586 €
■ UNIGE	571 618 €
■ UL	604 728 €
■ IVSAS	528 866 €
■ UNIVMED	888 404 €
■ EVA Management	700 719 €
Total	6 985 701€

# EVA organization



# EVA: european network of 9 high calibre laboratories

- 1- **EPV** (Associated lab IRD/Univ)-COVIBIO,(Prof Xavier deLamballerie), Marseille, France
- 2- **Veterinary Laboratories Agency** (T Fooks), United Kingdom
- 3- **Virology laboratory-P4 network**, Bernard Nocht institut für Tropenmedizin (Prof Stephan Günther), Hamburg, Germany
- 4- **Virology laboratory** (Prof Christian Drosten), Bonn Univ, Germany
- 5- **National Collection of Pathogenic Viruses** (David Lewis), Salisbury, United Kingdom
- 6- **Department of Pathology and Immunology** (Prof Daniel Pinschewer), Geneva, Switzerland
- 7- **Institute of Microbiology and Immunology** (Prof Tatjana Avsic-Zupanc), Ljubljana, Slovenia
- 8- **Institute of Virology** (Prof Boris Klempa), Bratislava, Slovakia
- 9- **AFMB**, Protein production platform (Dr B Coutard), Marseille, France

# A permanent scientific advisory board

- **Professor Ernest Gould**, (President of the board)  
Former director of the Institute of Virology, Oxford (now known as CEH Oxford), United Kingdom.
- **Professor Rolf Zinkernagel**,  
Nobel laureate in Physiology or Medicine 1996. Director of the department of Pathology, Institute of Experimental Immunology, University Hospital of Zurich, Switzerland
- **Professor Robert Tesh**  
Director of the World Reference Center of Emerging Viruses and Arboviruses. University of Texas, Medical Branch, Galveston, Texas.
- **Doctor Jan ter Meulen**  
Executive Director for vaccines development, Merck, West Point, USA
- **Professor Richard Elliott**  
Director of the Center for Biomolecular Sciences, School of Biology, University of St Andrews, Scotland.
- **Doctor Peter Daniels**  
Director of the Australian Animal Health Institute, Geelong Vic, Australia
- **Doctor Katrin Leitmeyer**  
Representative of the European Centre for Disease Prevention and Control, Stockholm, Sweden (E-CDC)

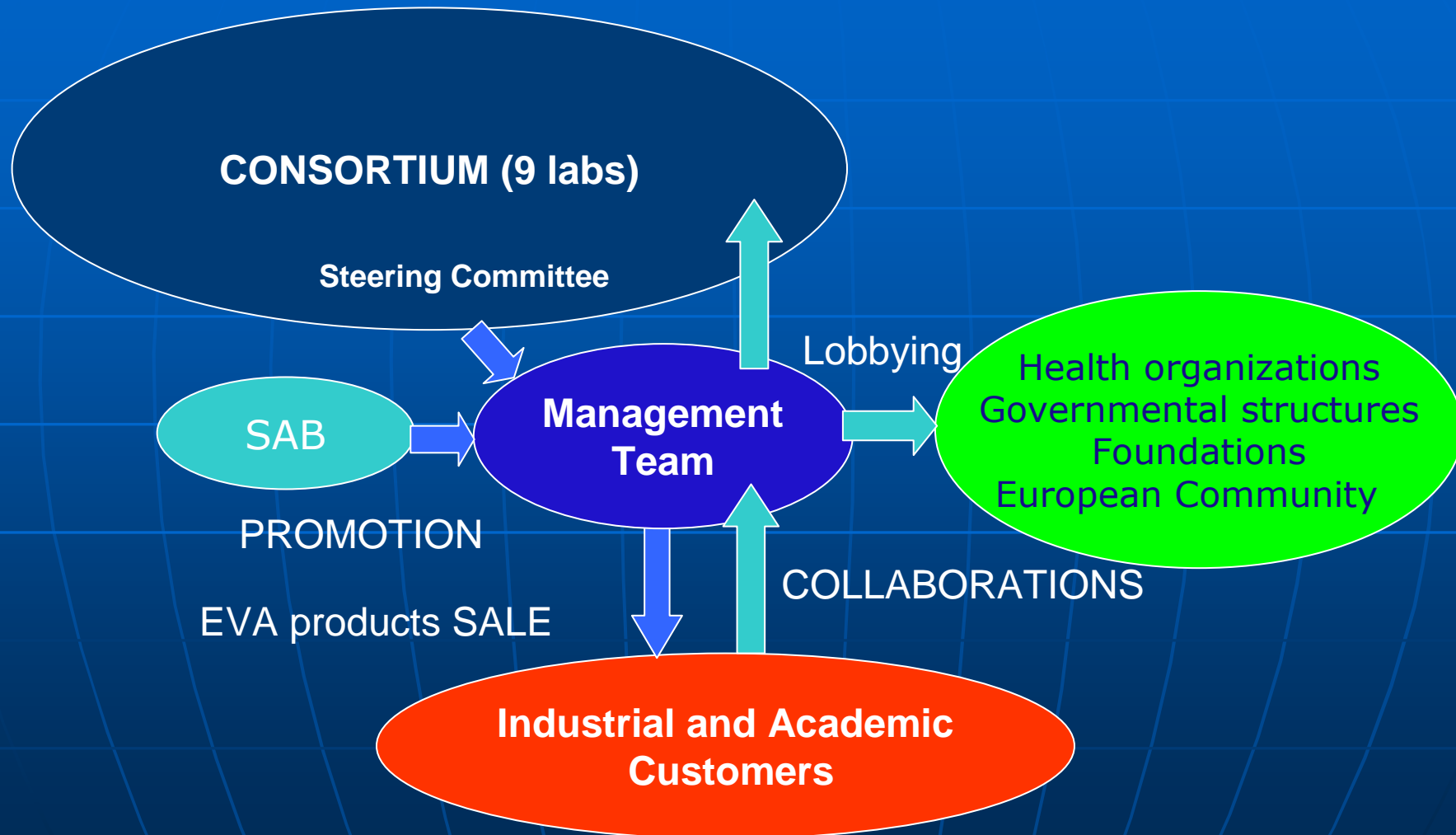
# Institutional links with international collections

- **Center for Biodefense & Emerging Infectious Diseases**, Galverston, Texas, USA
- **CSIRO**, Geelong Vic, Australia
- **Massey University**, Palmerston, New Zealand
- **Institute of Microbiology**, Academia Sinica, Beijing, China
- **ARC- Onderstepoort Veterinary Institute**, Pretoria, South Africa
- **IRD** networks, Marseille, France
- **Russian Collections** (on process)

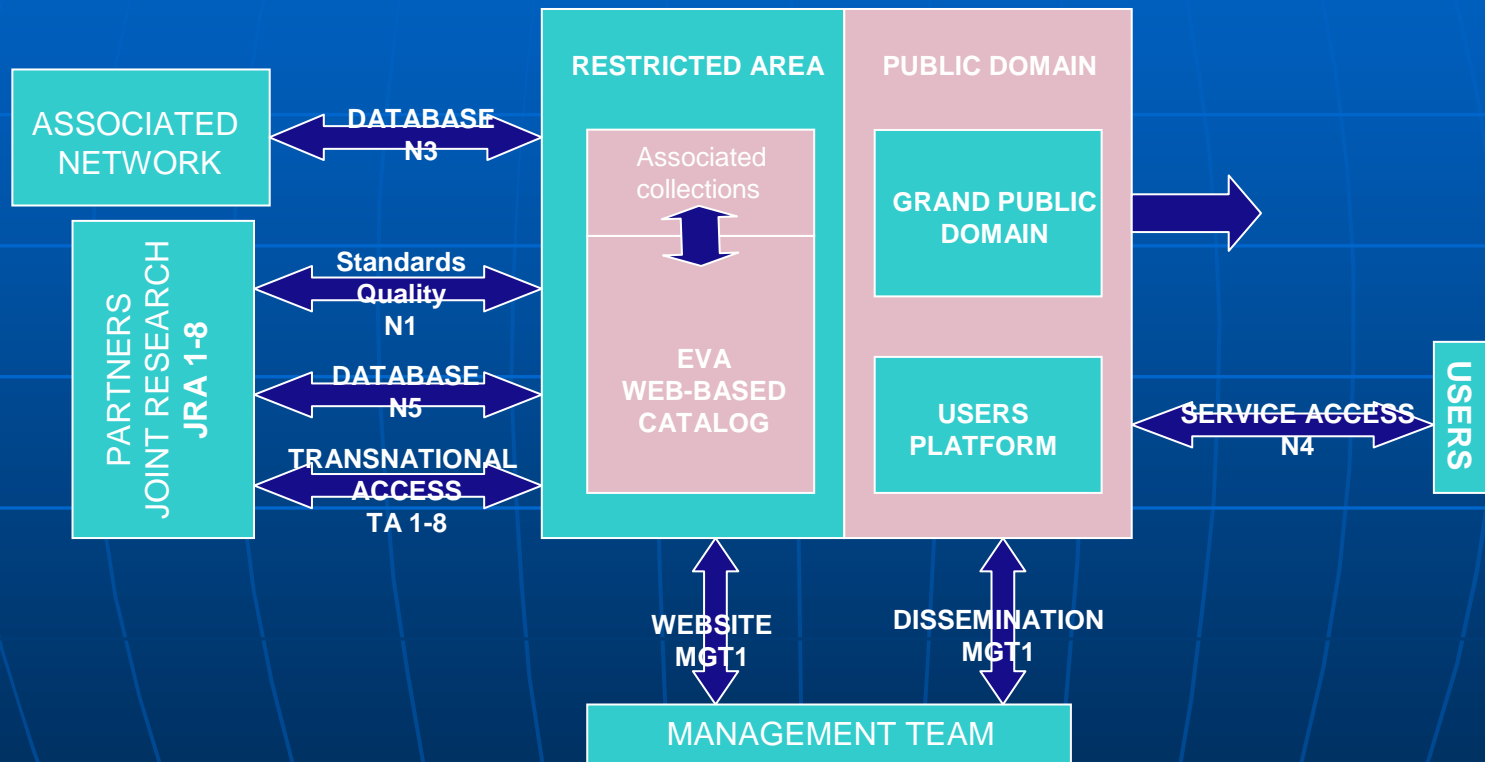
## EVA consortium foundation

- Each partner retains ownership of its biological resource
- Each partner is free to decide which part of its collection will be shared with the consortium
- EVA management has been mandated to represent EVA partners for all actions aiming at
  - Developing networks with new associated partners
  - Promoting EVA consortium activities and results
  - Giving access to EVA biological resources
- All partners have signed a consortium agreement defining rights and duties

# EVA management organization



EVA  
WEBSITE  
N5



# EVA objectives

# 250 viral species, more than 12000 viral strains: the largest collection worldwide

VIRUS FAMILY	P1	P2	P3	P4	P5	P6	P7	P8
<b>BSL2/3 virus</b>								
Flavivirus	x	x		x	x		x	x
Togavirus	x	x		x	x			x
Picornavirus	x	x		x	x	x		
Arenavirus	x	x			x	x		
Bunyavirus	x	x			x		x	x
Reovirus	x	x			x	x		x
Rhabdovirus		x		x	x	x		
Ortho/Paramyxovirus	x	x		x	x	x		
Poxvirus		x			x	x		
Herpes virus	x	x		x	x	x		
Coronavirus		x		x	x			
Arterivirus						x		
Veterinary virus (other)		x						
Parvovirus				x				
Adenovirus				x	x	x		
Astrovirus					x			
<b>BSL4 virus</b>			x					



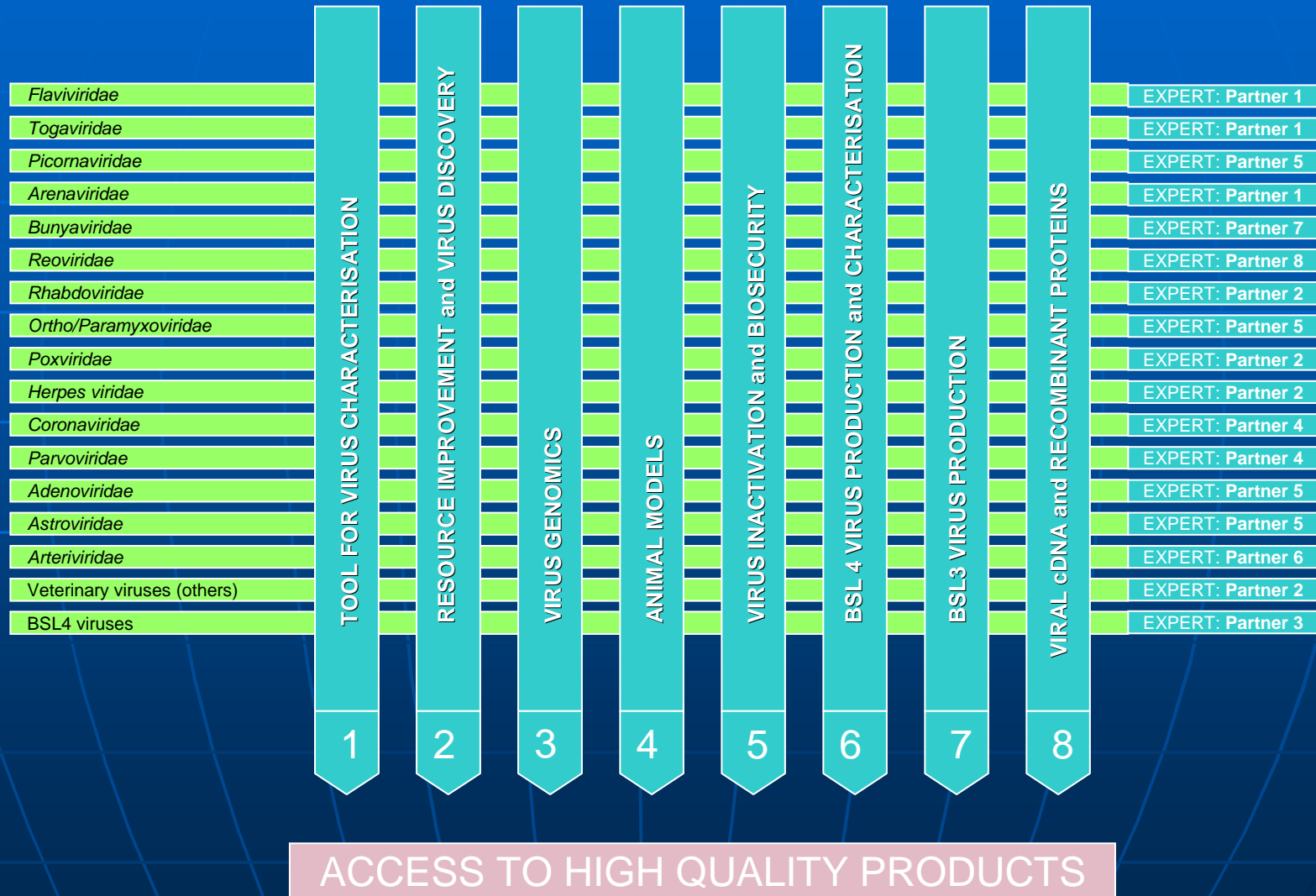
Virus family leader



## **EVA missions: to deliver first quality products through a professional organization**

- Quality of the resources: characterized human and veterinary viruses
- Quality of the storage conditions to preserve recent clinical isolates
- GMP: Biological Resource Centre's standards
- Quality of the service: BSEN ISO 9001:2008
- Supply of viral derived products: antibodies and purified viral proteins, PCR products...

# Tasks organization



# List of detected viruses (1)

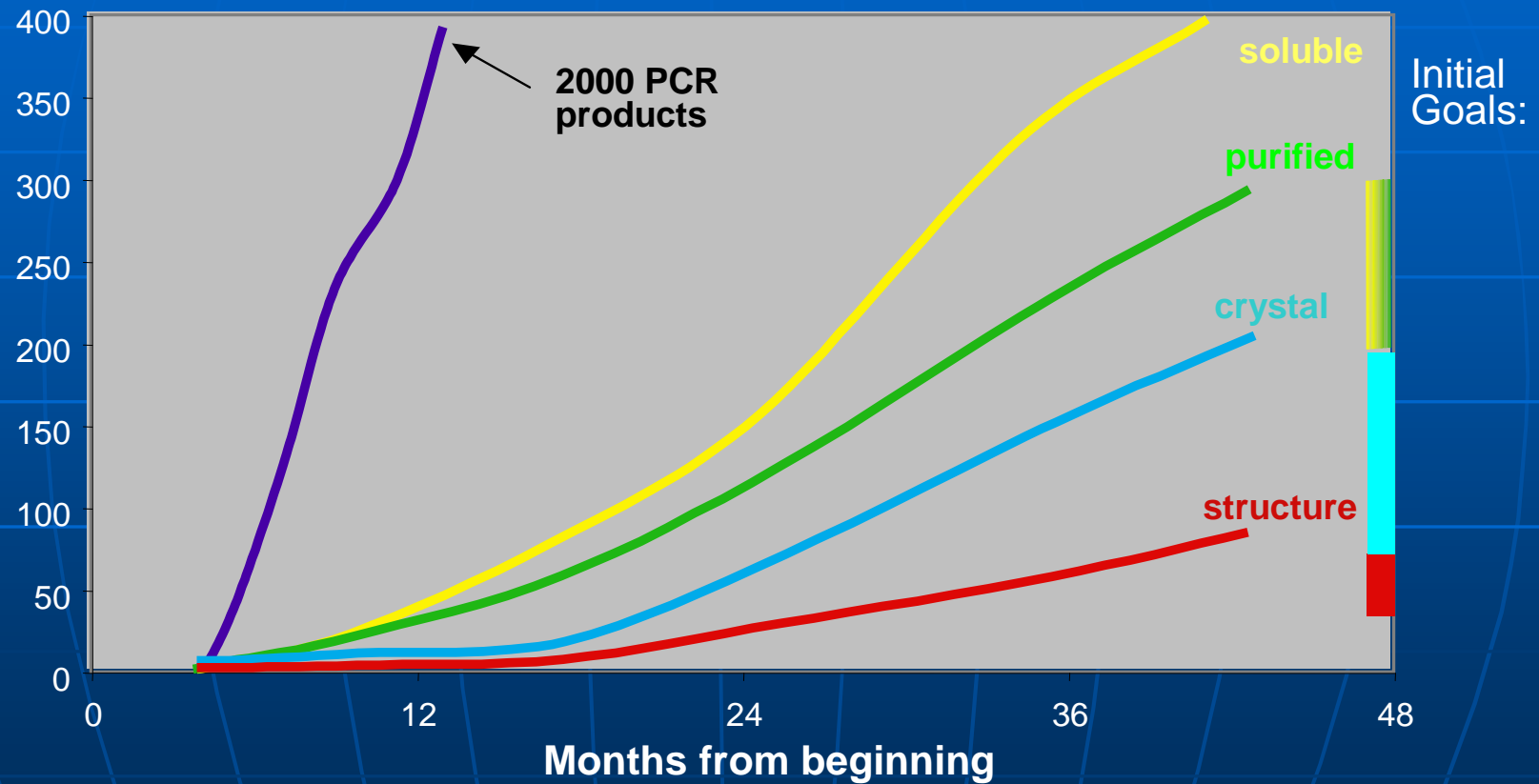
virus	TaqMan probe	Sybr Green	Synthetic primer	Not probe
BK	◆			
Boravirus				
Chikungunya	◆			◆
Lymphochoriomeningitis		◆		
Cimeacomp	.			
Cytomegalovirus	◆			◆
dengue 1	◆		◆	
dengue 1-4	◆		◆	
dengue 2	◆		◆	
dengue 3	◆		◆	
dengue 4	◆		◆	
Ebola				
Japanese encephalitis	.			◆
Enterovirus 71	◆			◆
Yellow fever	◆			
Flavivirus (universal)		◆	◆	◆
GAPDH	◆			
A fu	◆			◆
B fu	◆			◆
H1 flu	.			
H3 flu	.			
H5 flu	◆		◆	◆
Hendra				
Herpes simplex virus	◆			◆
HHV-6	◆			
HHV-8	◆			

## List of detected viruses (2)

JC-BK	◆		
Marburg			
Metapneumovirus	◆		◆
Mycoplasma	◆		
Nipah			
Norovirus genotype I	◆		
Norovirus genotype II	◆		
Onyong nyong	◆		◆
Measles	◆		◆
Orthopoxvirus			
Parvovirus B19	◆		
phage MS2	◆		
phage T4	◆		
Rabies	◆		◆
Rhinovirus	◆		◆
Rift valley fever virus	◆		
Rotavirus	◆		
Mumps	◆		◆
Rubella	.		
SARS Coronavirus	◆	◆	
tick-borne encephalitis virus	.	.	
Toscana	◆		
Varicella	◆		◆
Small pox			
VRS-A	◆		◆
VRS-B	◆		◆
West Nile	◆		

◆, routinely; ◆, under development.

# From the VIZIER project



ARN viruses data for antiviral drug design...

# Also: To be prepared against Emerging viruses

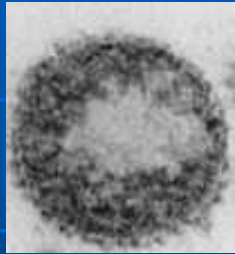
**EPIDEMY**

MONONEGAVIRALES

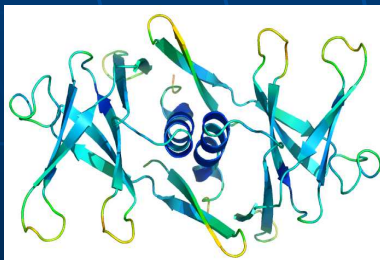
*Bornaviridae*

*Filoviridae*

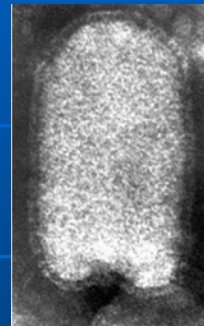
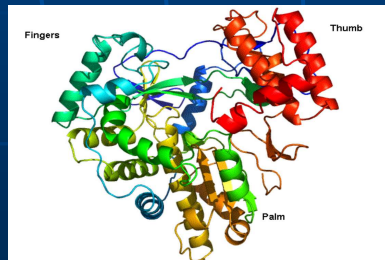
*Rhabdoviridae*



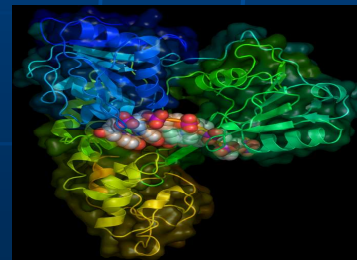
Borna disease



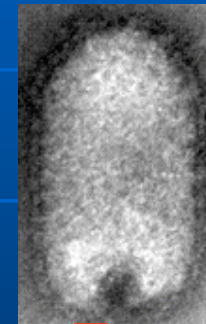
Ebola



Rabies



**Emerging Virus**



**Signatures...  
Predicted drug...  
Predicted structure.  
Faster answer...**

END

# EVA QMS objectives for consortium partners

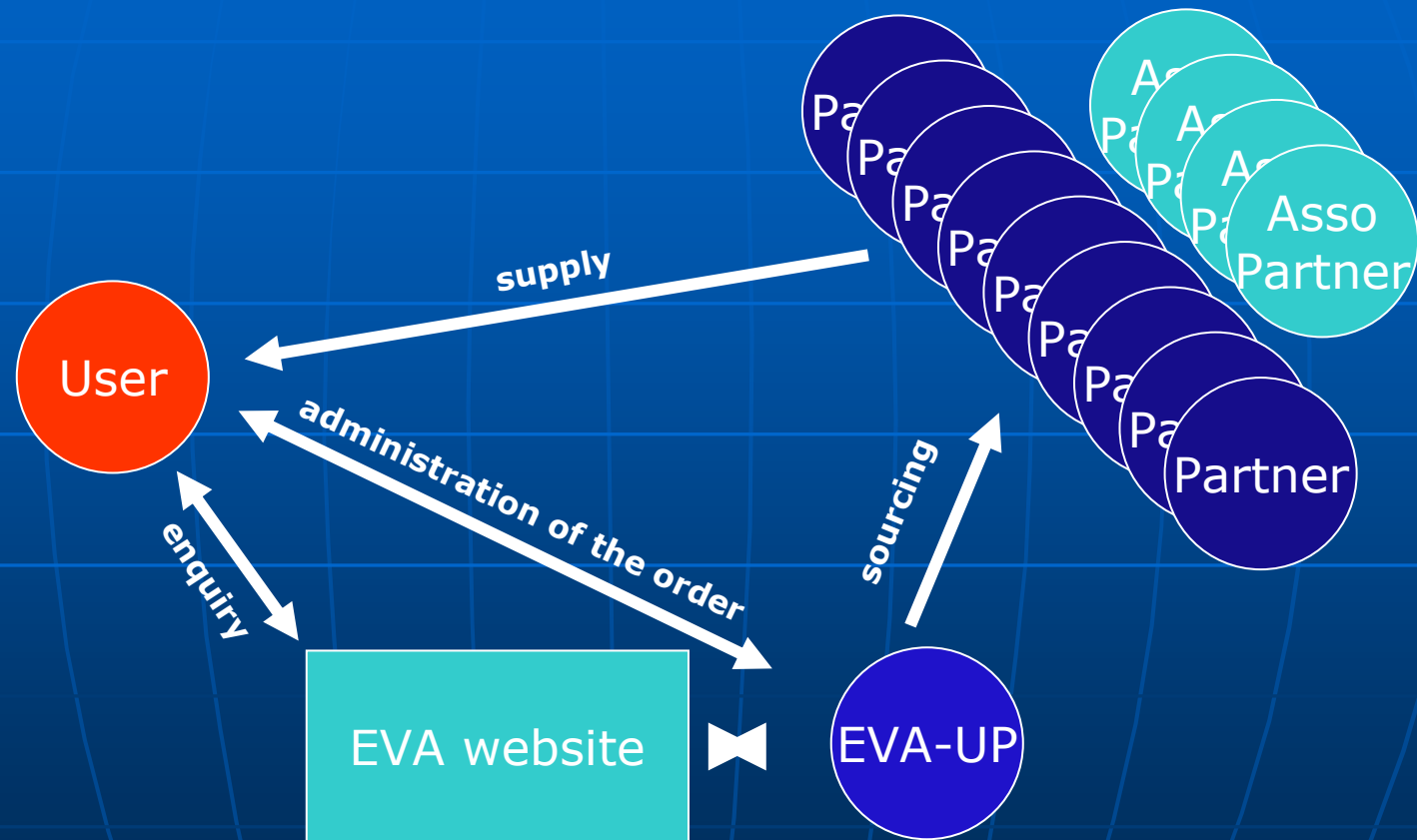
- Define and establish a set of best practice quality guidelines for adoption by the consortium partner collections.
- Improve QMS standards across the consortium partner collections
- Guarantee the quality, purity and identity of resource provided to users through the EVA partnership
- Harmonised service levels across the consortium.



# EVA-Users Platform: EVA-UP

- Division of the Management team, in charge of the Intellectual property, managed by the coordinator of the project
- A legal entity, third party of one of the EVA partner institution (UNIVMED)
- Unique interface between Consortium partners and users
- In charge of the maintenance of the EVA-website public domain
- Mandated by EVA partners to administrate the orders related to the EVA products and service

# Management of orders



Simple and efficient procedure to reduce delivery time

# EVA-UP

## a unique point to entry the consortium

- Access to EVA biological resource is organised via the EVA-UP:
  - Supply of viruses
    - Grade 1: fully characterized, full genome sequence
    - Grade 2: fully characterized, sequence of main locus (fragmented genome)
    - Grade 3: fully characterized, partial genome sequence
  - Supply of cell lineages and production protocols
  - Supply of PCR products on request
  - Supply of soluble viral proteins
  - Supply of crystallized viral proteins (X ray diffraction studies on request)
- Collaboration contracts with EVA partners are drafted by EVA-UP

# Access to EVA resource managed by EVA-UP

- Intellectual property and bio-safety
  - Material Transfer Agreement form with a technical annex describing the intended use of the material by the recipient
  - Qualification certificate given by the National Security Service to the recipient institution/organization, describing the facilities where the material will be used. Bio-safety level of laboratories should be clearly identified.
- Financial aspects related to the material
  - A quotation will be prepared accordingly to the enquiry and sent to the user
  - A purchase order with bank references and commercial ID number will be received prior to the material delivery
  - Delivery will be organized by courier companies qualified for this type of shipment
- User identification
  - In addition, verifications will be made to secure the user identification like e-mail address (no generic addresses but institution addresses), direct exchanges via e-mail with the recipient
  - For critical supply, the National Security Service will be informed, before the shipment of the viruses, and confirmation will be obtain for the delivery.

## EVA-UP Products Prices

- Grade 1-3, P3 Virus from 250 to 500€
- Grade 1-3, P4 Virus from 1500 to 2000€
- Specific quotation for others products: PCR products, proteins, cells
- 20% of the supplies are delivered free of charge to academic and EVA-associated institutions (fully supported by EU)

# The VIZIER project & the VIP

FP6 Scientific Integrated Project (2004-2008)

OR

**Preparing Europe for the Next Viral Outbreak**

**Jean-Louis ROMETTE**

Professor

VIZIER, IPR and Exploitation manager

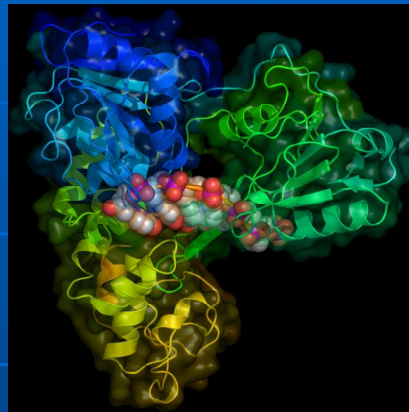
VIZIER Industrial Platform director

AFMB, CNRS/University of Marseille

France

# What is VIZIER?: Viral enZymes InvolvEd in Replication

Goal : Identification of new targets from RNA viruses through a structural characterization of the replicative system



Structural Genomics project supported by the European Union

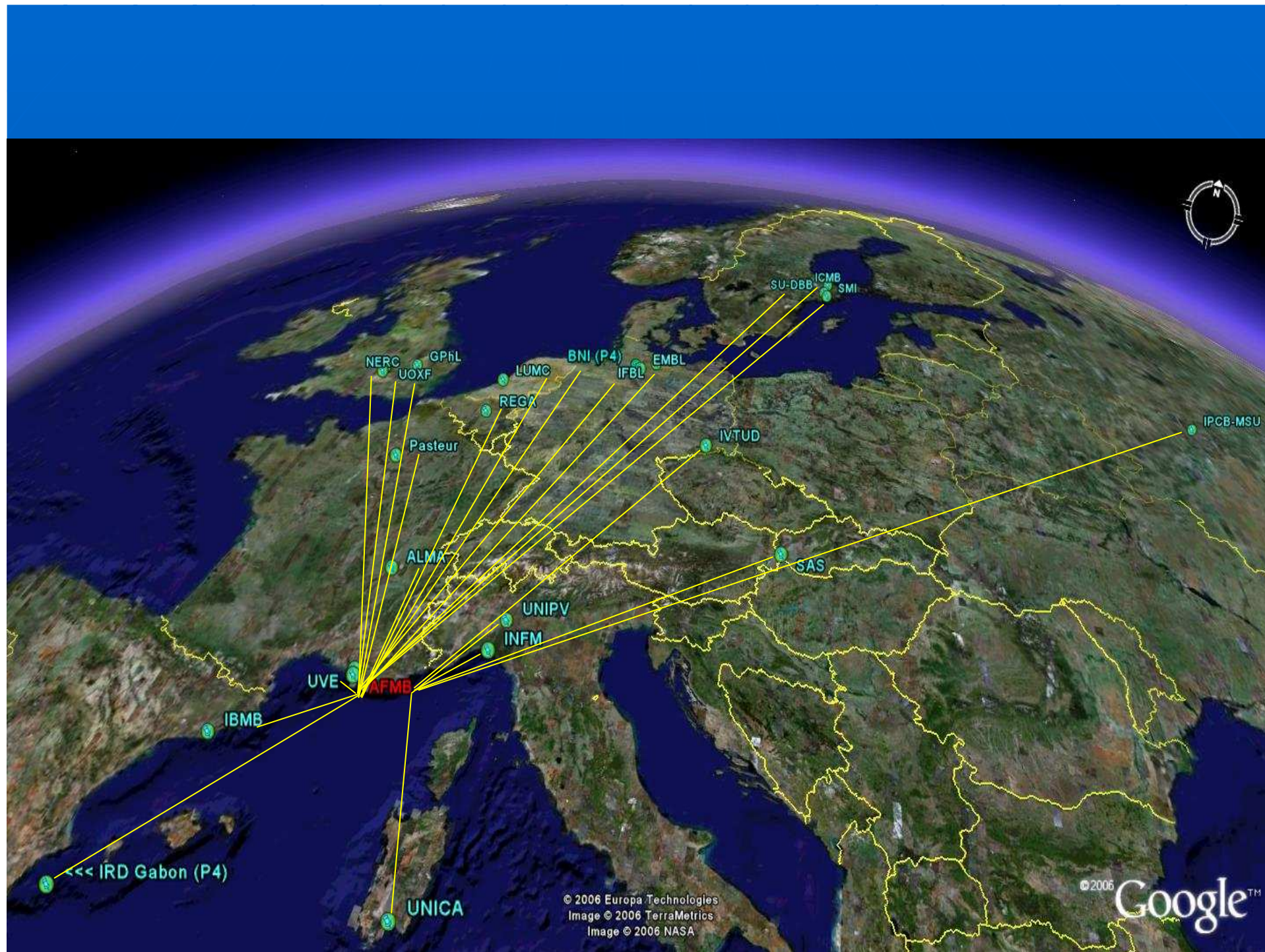
Started in November 2004 up to (at least) October 2008

Means :           23 “partners” (public research centers)  
                      >100 full time researchers involved  
                      13 M€ funding by EEC



	Gadgets Gully virus	Kadipiro virus	Puumala virus
	Guanarito virus	Kamiti River virus	Rabbit haemorrhagic dis.virus
	Hantaan virus	Karshi virus	Rabies virus
Allpahuayo virus	Hepatitis A virus	Kedougou virus	Rio Bravo virus
Alfuy virus	Hepatitis C virus species	Kokobera virus	Sabia virus
Alkurma virus	Hepatitis E virus	Kunjin virus	Saboya virus
Amapari virus	Human astrovirus Type 1	Kyasanur Forest disease virus	Saint Louis encephalitis virus
Apoi virus	Human astrovirus Type 4	Langat virus	Sapovirus
Australian bat lyssavirus	Human coronavirus	Lassa virus	Semliki Forest virus
Avian infectious bronchitis virus	Human coxsackievirus A9	Latino virus	Sendai virus
Bagaza virus	Human coxsackievirus B2	Louping ill virus	Seoul virus
Banna virus	Human coxsackievirus B3	Lymantria dispar cypovirus 1	Sepik virus
Bear Canyon virus	Human coxsackievirus B5	Lymantria dispar cypovirus 14	SARS coronavirus
Bombyx mori cypovirus 1	Human echovirus 11	Lymphocytic choriomeningitis virus	Simian hemorrhagic fever virus
Bussuquara virus	Human echovirus 13	Machupo virus	Sindbis virus
Cell fusing agent virus	Human echovirus 18	Mammalian orthoreovirus 1	Spondweni virus
Cell silent agent virus	Human echovirus 30	Meaban virus	Tamana bat virus
Chikungunya virus	Human echovirus 6	Measles virus	Tamiami virus
Chum salmon reovirus	Human echovirus 7	Modoc virus	Tembusu virus
Colorado tick fever virus	Human enterovirus B	Mokola virus	Tick borne encephalitis virus
Cupixi virus	Human enterovirus C	Montana myotis leukoencephalitis virus	Transmissible gastroenter. virus
Dengue virus 1	Human enterovirus D	Mopeia virus	Trichoplusia ni cp virus 15
Dengue virus 2	Human respiratory syncytial virus	Murine hepatitis virus	Tula virus
Dobrava virus	Human respiratory syncytial virus A2	Murray Valley encephalitis virus	Tyulenii virus
Eastern equine encephalitis virus	Human rhinovirus B	Ngoye virus	Uganda S virus
Edge Hill virus	Iguape virus	Norovirus	Usutu virus
Enterovirus	Inachis io cypovirus 2	Oliveros virus	Venezuelan equine encephalitis virus
Enterovirus 76	Infectious bursal disease virus	Omsk hemorrhagic fever virus	Vesicular stomatitis Indianavirus
Enterovirus 93	Infectious pancreatic necrosis virus	Orgyia pseudotsugata cp virus	Wesselsbron virus
Enterovirus 94	Influenza A virus	Parana virus	West Nile virus
Equine arteritis virus	Influenza A virus	Peruvian horsesickness virus	Western equine encephalit. virus
Equine torovirus	Ippy virus	Porcine r&r syndrome virus	Yellow fever virus
Feline infectious peritonitis virus	Japanese encephalitis virus	Potiskum virus	Yokose virus
	Kadam virus	Potiskum virus	Zaire ebola virus
		Powassan virus	Zika virus





## European opportunities

- The European integrated project VIZIER
- An active European network of virologists
- European Commission funding (Infrastructure call)
- A strong demand from industrial and academic research laboratories