ABSA, 60th Annual Biological Safety Conference
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A journey of biological risks between compliance and risk optimisation

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ERG
Safer Together

Acknowledgement

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Note: This presentation is not expressing the opinions of Merck or MSD.

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The Elizabeth R Griffin Research Foundation
http://www.ergriffinresearch.org/

EUFMD Biorisk Committee
European Commission for the Control of Foot and Mouth Disease

International Veterinary Biosafety Workgroup
www.ivbw.camp9.org

OIE ad hoc group for biosafety

European Biosafety Association
www.ebsaweb.eu

Epibiosafe
www.epibiosafe.com

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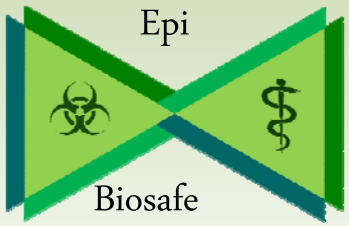
Introduction

Where are we heading? What are the challenges?



Sustainable Biosafety Goals 2030

GLOBAL CONFERENCE ON BIOLOGICAL THREAT REDUCTION

Building cooperation for efficient health and security systems worldwide

30 JUNE – 2 JULY 2015

MAISON DE LA CHIMIE, PARIS

Global Health Security Agenda

Prevent	1	Antimicrobial Resistance Action Package
	2	Zoonotic Disease Action Package
	3	Biosafety and Biosecurity Action Package
	4	Immunization Action Package
Detect	1	National Laboratory System Action Package
	2/3	Real-Time Surveillance Action Package
	3	Reporting Action Package
	4	Workforce Development Action Package
	5	Emergency Operations Centers Action Package
Respond	1	Emergency Operations Centers Action Package
	2	Linking Public Health with Law and Multisectoral Rapid Response Action Package
	3	Medical Countermeasures and Personnel Deployment Action Package

GHSA: Prevent 3- Biosafety and Biosecurity

- **Target:** A whole-of-government national biosafety and biosecurity system is in place, ensuring that especially dangerous pathogens are identified, held, secured and monitored in a minimal number of facilities according to best practices; biological risk management training and educational outreach are conducted to promote a shared culture of responsibility, reduce dual use risks, mitigate biological proliferation and deliberate use threats, and ensure safe transfer of biological agents; and country-specific biosafety and biosecurity legislation, laboratory licensing, and pathogen control measures are in place as appropriate.
- **Desired National Impact:** Implementation of a comprehensive, sustainable and legally embedded national oversight program for biosafety and biosecurity, including the safe and secure use, storage, disposal, and containment of pathogens found in laboratories and a minimal number of holdings across the country, including research, diagnostic and biotechnology facilities. A cadre of biological risk management experts possesses the skillset to train others within their respective institutions. Strengthened, sustainable biological risk management best practices are in place using common educational materials. Rapid and culture-free diagnostics are promoted as a facet of biological risk management. The transport of infectious substances will also be taken into account.

Challenge

- Biosafety is often portrayed as a binary (on or off) compliance function.

As a consequence people want to staff it as a compliance function, low qualification, low salary, but high expectations.

Sustainability – what is sustainable biosafety?

- Responsible use of **energy** and **consumables**
- The facility is resourced to **maintain** all biosafety protection layers out of its core budget.
- Safety systems are maintained for **low operating costs** and long useful live cycles
- The application of the controls is **long term viable** and not dependent on short term extra funding.
- The cost of the control is **proportionate** to the protection required
- The risk to the operator and environment is control with proportionate “force”

Human Factors

- Management accountability
- Training
- Ergonomics
- Social Control
- Engineering controls
- Risk assessment
- Business continuity

- … human factor analysis needs to be much more embedded in our concepts.

2030 Biosafety Themes

People

- Competencies
- Accountability
- Biorisk Management Culture
- Roles and Responsibilities
- Occupational Health
- High Reliability Organisations

Processes

- Risk Management
- Learning /Knowledge sharing
- Setting acceptable residual risk levels
- Measure Safety Performance
- Taking biological risk management from the lab to the field
- Sustainability

Facilities

- Fit for purpose
- Attractive to work in
- Low carbon foot print
- Affordable
- Simplicity
- Reliability
- Certification to relevant performance criteria

Science

- **Why**
- **Data**
- Capability
- Capacity
- Accountability

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Compliance and risk assessment - *the case of Rinderpest*

Rinderpest

- >90% mortality in cattle
- Most closely related to measles
- Rinderpest eliminated from Europe entirely through biosecurity
- Introduced to Africa in late 1800s
- Annual cost to Africa was >1 billion USD/yr
- Foundation of the OIE
- Development of vaccines
- 40 years of eradication from 1970 to 2010

Early days of biological risk assessment and compliance

- 18th century:
  - First animal disease control legislation:
  - First veterinary schools in Europe
- 20th century science led developments in biosafety and biocontainment little legislation.
- 21st century tension between compliance and science led biosafety.

Rinderpest the animal disease curse of Europe 1600 to 1850.

- famines due to the loss of draft oxen
- Periodic import from Eastern Europe/Asia
- first legislation 1714-17 (France, Prussia, Austria, Italy)
- capital punishment for movement of cattle In Italy
- One of the drivers for the first vet schools

Biosecurity concepts:

- cordon sanitaire,
- movement bans
- stamping out,
- isolation in time
- military charged to enforce rules
- transmission from infected animals and animal materials

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Development of containment measures

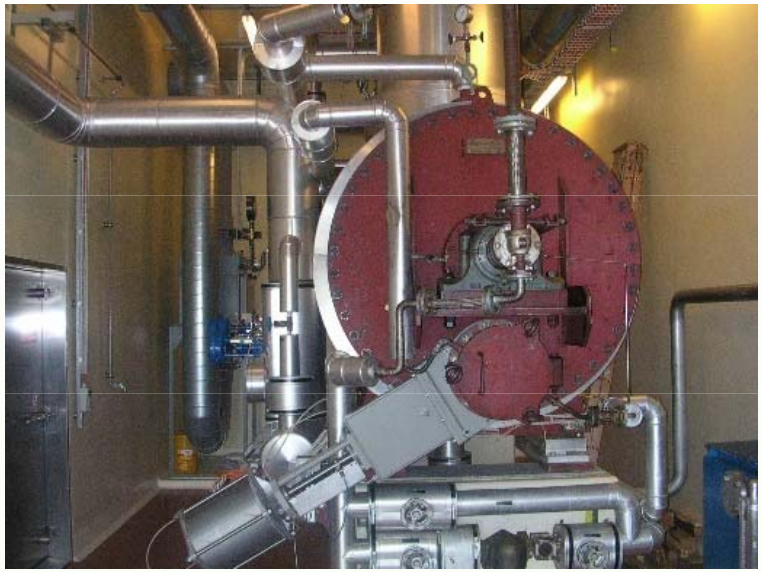
Vaccine Institute Basel
Institut fédéral des vaccins Bâle

- 13. June 1917 Federal Law for the control of Animal diseases empowers the government to establish facilities for the investigation of and diagnosis of animal diseases and collect money for this from the cantons
- 25 June 1921 Motion to establish a facility is approved in the federal council
- 2 Feb 1939 further motion to build such a facility
- 1939 Expert committee reports on the requirements. No colocation with other research facilities, proximity to an abattoir,
- 6th Feb 1941: budget and location approved
- Sept 1941: Construction begin
- 26 Oct 1942: Official Opening Ceremony
- *1992 transferred to Mittelhäusern*

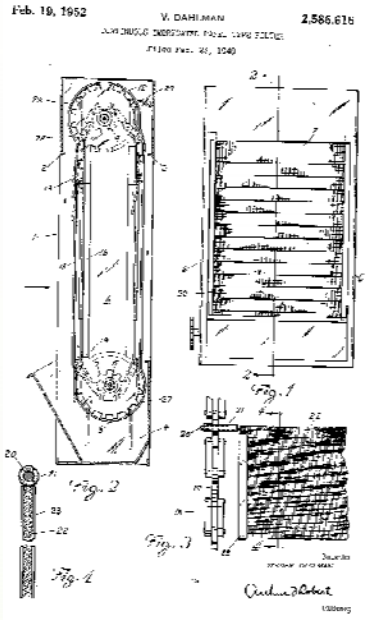
Biocontainment features in the first Swiss foot and mouth vaccine facility in 1942

Eidgenössisches Vakzine-Institut Basel

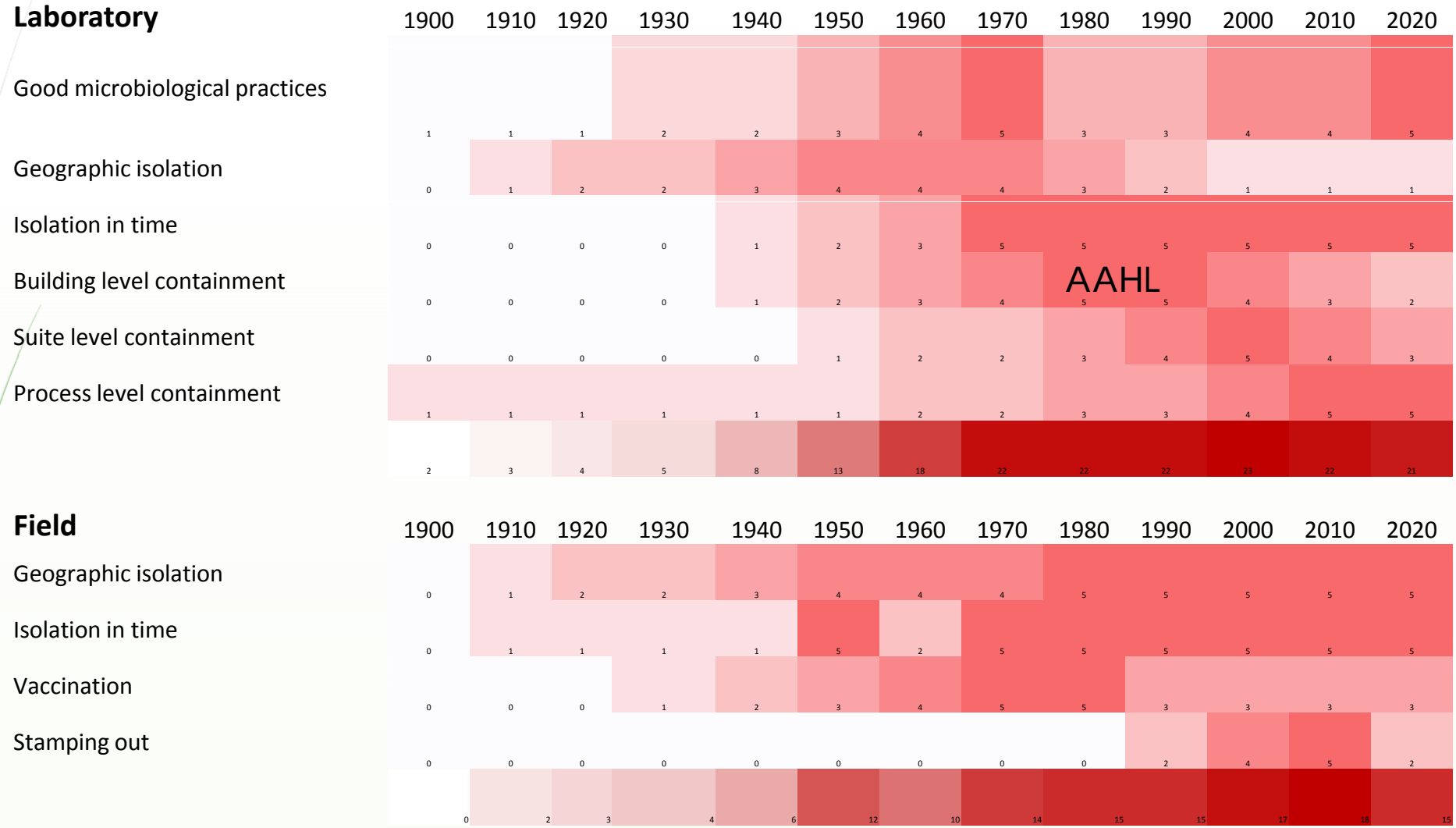
- Effluent treatment (80°C 20 minutes)
- Air filtration (ölbenetzte Umlauffilter)
- Barrier personnel showers with supervision
- Barrier autoclave, barrier disinfection
- Strict separation in clean and unclean zones
- Underpressure to achieve inward directional airflow
- Management of waste, carcass disposal



Oil bath type filters (ölbenetzte Umlauffilter)



Changing Emphasis of Control Measures



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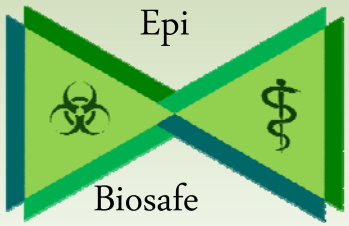
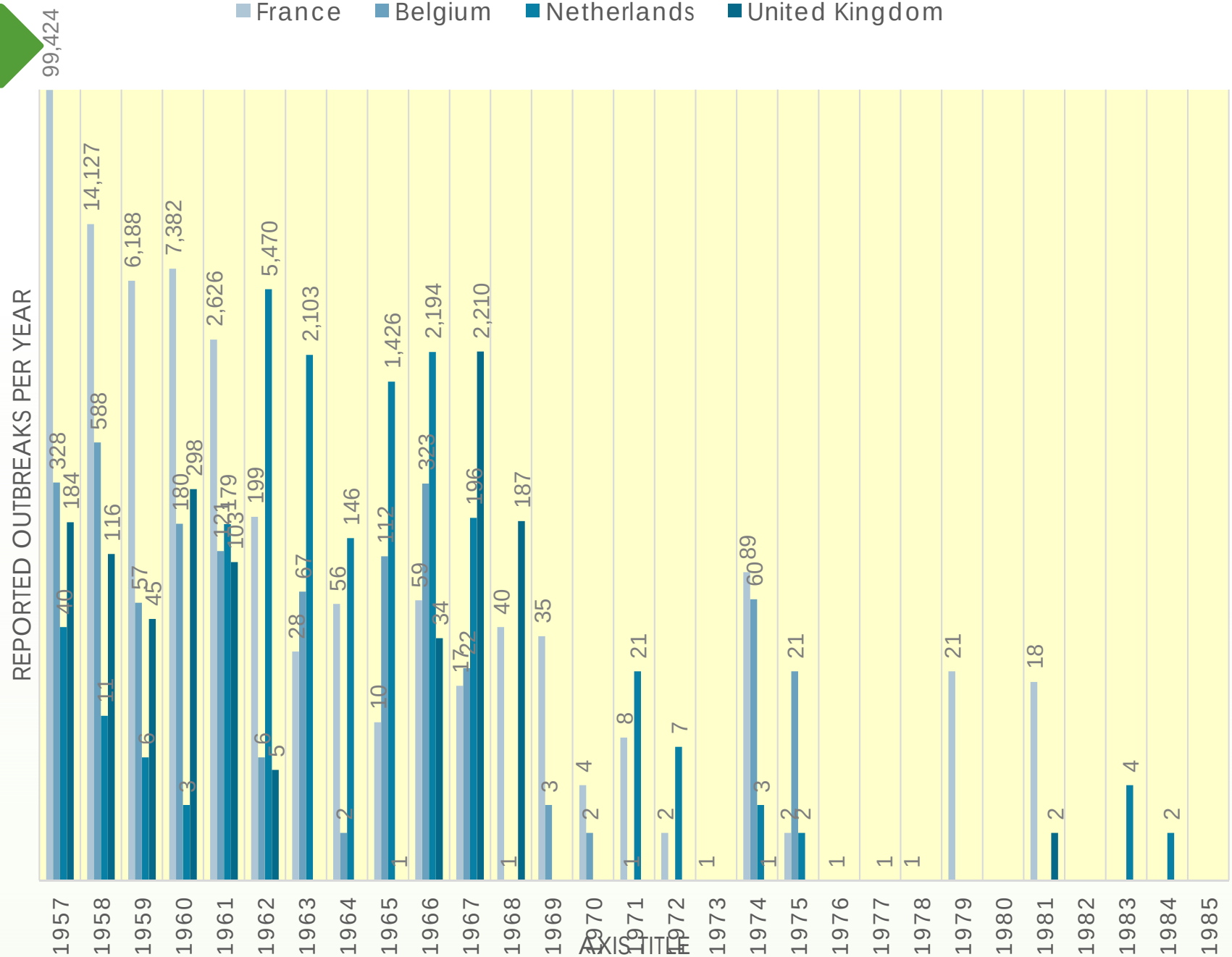
Case Study

Requirements for facilities handling FMDV - compliance driven improvements



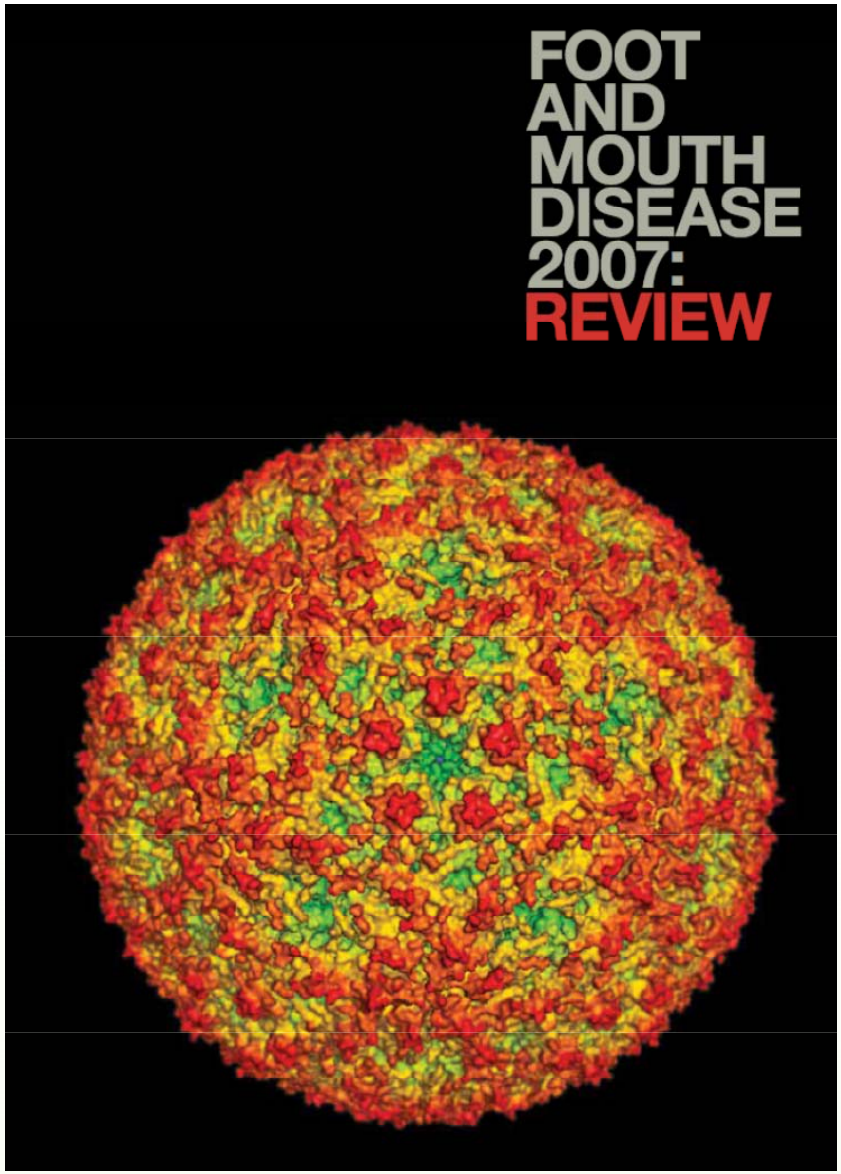
FMDV OUTBREAKS IN EUROPE



Rev. sci. tech. Off. int. Epiz., 1986, **5** (2), 271-277.

Facility/vaccine related outbreaks

Year	Country
1960	UK
1968	Denmark
1969	Czechoslovakia
1972	Hungary
1974	Germany
1975	Czechoslovakia
1977	Germany
1977	Germany
1979	Spain
1987	Germany
1988	Germany
1993	Russia
2007	UK
2016	Russia



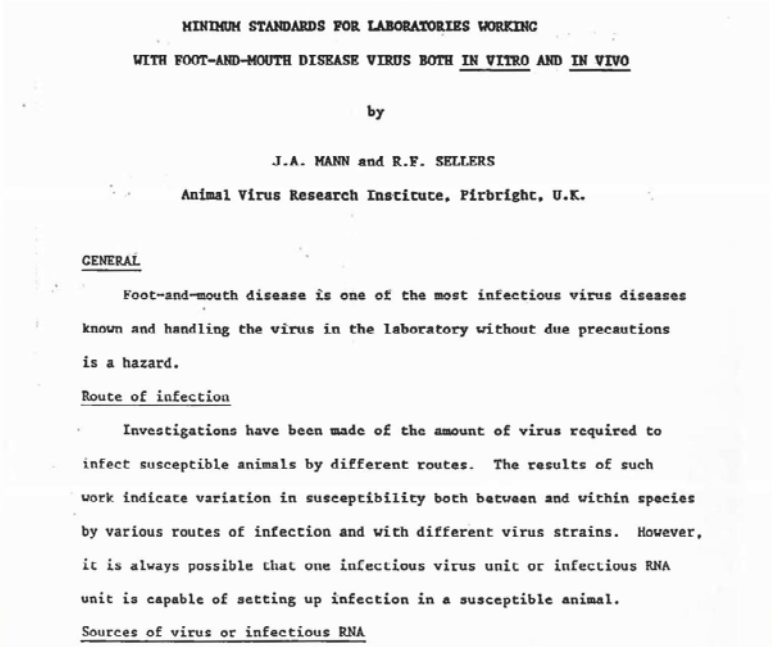
Rethinking priorities at the end of the European FMD era

The eradication by mass vaccination and import controls was so successful that by the 1980s Western Europe was essentially free of the disease.

Enough to recognise that vaccine failures and facility failures were making up the majority of the disease signal.

This lead to a major policy change:

- Stop routine vaccination development of antigen banks
- Reduced number of facilities
- Improved safety standards for FMDV facilities



MINIMUM STANDARDS FOR LABORATORIES WORKING

WITH FOOT-AND-MOUTH DISEASE VIRUS BOTH IN VITRO AND IN VIVO

by

J.A. MANN and R.F. SELLERS

Animal Virus Research Institute, Pirbright, U.K.

GENERAL

Foot-and-mouth disease is one of the most infectious virus diseases known and handling the virus in the laboratory without due precautions is a hazard.

Route of infection

Investigations have been made of the amount of virus required to infect susceptible animals by different routes. The results of such work indicate variation in susceptibility both between and within species by various routes of infection and with different virus strains. However, it is always possible that one infectious virus unit or infectious RNA unit is capable of setting up infection in a susceptible animal.

Sources of virus or infectious RNA

Foot and Mouth Disease as a driving force for regulation and setting of safety standards

1954	European Commission for the Control of FMDV is founded
1985	EUFMD Minimum Standards drafted - *facilities and vaccine failures posed the main disease threat*
1990	FMDV Vaccination is stopped in Europe
1993	EUFMD Minimum Security Standards updated
2003	Minimum Security Standards included in FMDV Directive
2009	MS revised to include biological risk management system principles
2009	- 2012 European Commission inspects all FMDV labs against Minimum Standards
2013	Inclusion of Contingency Laboratories in EUFMD Minimum Biorisk Management Standards.

Minimum Biorisk Management Standards for Facilities handling Foot and Mouth Disease *in vitro* and *in vivo*

- Annex of the EU Foot and Mouth Disease Directive
- Only Europe wide veterinary biorisk management instrument
- Sets out requirements for a biological risk management system, so needs to be supported by a facility risk assessment
- Implementation under national oversight
- Written by practitioners as guidance, but has the status of a regulation
- 1993, 2009, 2013 versions

EU Food and Veterinary Office audits of FMDV facilities 2009-2012

		Audit Nr	CA performance			General and specific biosecurity requirements												Points
			Tl	C	Q	G	M	Tr	B	P	F	H	A	Ef	S	Em	D	
High activity FMD labs	Diagnostic and / or research labs	1	0	10+gp	10	40	40	40	20+gp	20	20	20	20	20	20	40	40	380
		2	0	40	20	20	20	40	20	40	40	40	20	40	20	40	20	420
		3	20	20	20	40	40	40	40	20	20	20	40	20	40	40	40	460
		4	0	40	40+gp	20	20	20	40	40	20	40	40	0	40	40	40	450
		5	40	10	10	10	10	40	40	20	20	10	20	0	40	40	40	350
		6	40	0	10	10	20	40	20	20	10	10	0	10	0	20	20	230
		7	20	20	20	40	20	20	20	40	20	20	20	40	40	10	40	360
	Vaccine Production	8	0	10+gp	10	40	40	40	20+gp	20	20	20	20	20	20	40	40	380
		9	0	20	40	40	40	40	40	40	20	20	20	20	20	20	40	420
		10	20	40	40	40	40	40	40	40	20	40	20	0	40	10	40	470
		mean	14	23	33	30	29	36	32	30	21	24	22	17	28	30	36	392
Low activity FMD labs	Diagnostic labs	11	40	0	0	10	0	0	40	20	0	40	0	0	0	0	0	150
		12	20	40+gp	10	40	10	20	40	40	10	40	40	10	40	40	40	460
		13	40	0	10	10	10	10	40	40	40	20	0	20	40	0	10	290
		14	40	10	0	0	20	20	20	40	0	10	0	0	0	40	10	210
		15	0	0	0	10	10	10	40	10	10	10	40	0	0	10	40	190
		16	10	0	0	10	10	10	10	10	40	40	10	0	10	40	10	210
		17	40	10	0	10	40	10	20	40	20	0	10	10	40	20	10	280
		18	20	0	40	40	40	40	40	40	40	40	10	20	10	40	40	470
		19	10	0	0	20	40	20	10	20	40	20	10	40	40	10	20	300
		mean	24	8	9	17	19	16	27	29	22	27	9	11	19	22	20	256

FVO overview report

EU Food and Veterinary Office audits of FMDV facilities 2009-2012

- 19 facilities were inspected in 15 EU member states
- Some facilities had to stop the use of live FMDV due to non-compliance with the EU Minimum Standards
- Each EU member state has a laboratory for FMDV diagnosis or has contracted a laboratory in another member state.
- Some small non-compliant laboratories posed a smaller overall risk than some of the big players.
- The audit series leveraged funding for improvement in the majority of laboratories.

FVO overview report

Do we need live virus to maintain diagnostic proficiency?

- From 2003 onwards the World Reference Laboratory in Pirbright enhanced the diagnostic proficiency test panels to reduce the reliance on live virus handling for the demonstration of diagnostic proficiency.
  - Inactivated samples for PCR diagnosis
  - safety tested sera for serology
  - Inactivated antigens for antigen capture ELISAs
  - Armoured RNA assays for PCR detection proficiency

What were the options?

Option 1: Close down the non-compliant laboratories
Reduced capability for lab diagnosis based outbreak response

Option 2: Fund low income member states to upgrade their facilities to the FMDV standards.
Ongoing high operating costs

Option 3: Accept a lower risk reassurance level during outbreak response:

- *Virus is not handled in "peace times", no culture based diagnosis*
- *Modest costs to achieve the basic requirements*
- *Relative risk from the lab during an outbreak is much less than the risks from infected farms.*

Risk Based Minimum Standards

Tier	Purpose	Goal	Activities
Tier A (endemic)	Primary care front line "laboratory" in endemic setting	basic precautions, to reduce the likelihood of primary care contributing to enzootic burden and spread	Sample Collection & Clinical Care of herds
Tier B (endemic)	Specific diagnosis (laboratory serving region)	Perform primary diagnosis on FMDV in endemic setting; ability to ship materials internationally	Laboratory diagnosis using non replicating assays and or inactivated materials
Tier C (epidemic)	Tier C for endemic strains no infected animals	Perform primary diagnosis in acute epizootic setting, only current strains)	Tier C Outbreak Contingency Laboratories; no virus propagation; no infected animals
Tier D (Exotic)	R&D exotic strains, vaccine production	Safe handling of exotic strains where the residual risk is at least >10x smaller than the risk of natural incursion	Tier D Reference Laboratories and Research Facilities for exotic strains and Vaccine Manufacturers

Conclusion

- The EU accepted the risk based business case that facilities, which only handle inactivated materials for proficiency testing, have to meet a reduced set of criteria.
- Control measures in high containment are complex and prescriptive control measures are not enough.
- Facilities and Regulators are challenged to resource the oversight appropriately

"A world that is safe and secure from the accidental or deliberate release of animal pathogens, including zoonoses."

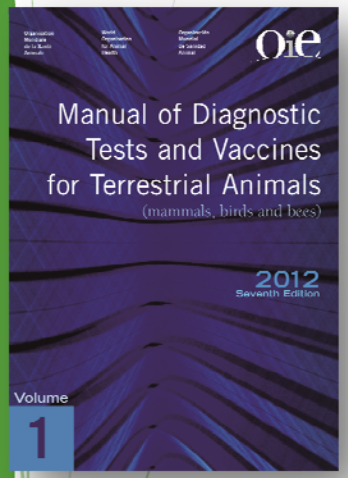
Office International des Epizooties

World Organisation for Animal Health

- *OIE sets international standards for animal health – adopted by the World Assembly of Delegates and applicable in all 180 Member Countries*
- capacity building allowing compliance with OIE standards and strengthening national veterinary services
- FAO/OIE/WHO work together (one health approach) for a comprehensive Biological Risk Management framework on human and animal health

OIE Biosafety and Biosecurity Resources

- OIE Standards -



A new chapter in the *Terrestrial Manual* was adopted as the current standard for member countries during the May 2015 General Session of the OIE:

Chapter 1.1.3.:

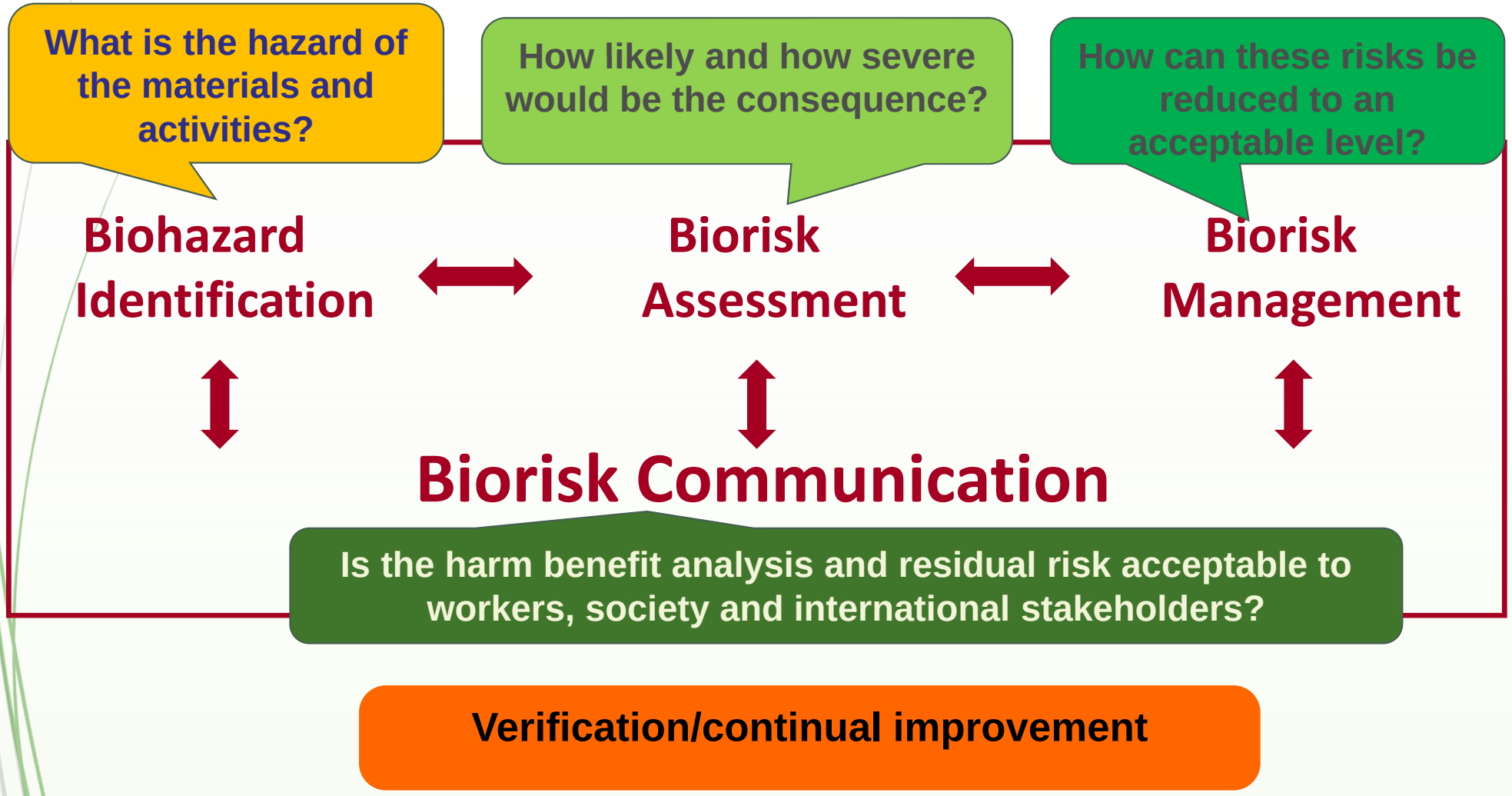
Biosafety and Biosecurity: Standard for Managing Biological Risk in the Veterinary Laboratory and Animal Facilities.

http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/1.01.3_BIOSAFETY_BIOSECURITY.pdf

Replacing Chapter 1.1.3., "Biosafety and biosecurity in the veterinary diagnostic microbiology laboratory and animal facilities".

Laboratory Biorisk Analysis

Biorisk Analysis is the process comprised of biohazard identification, biorisk assessment, biorisk management and biorisk communication.



"Challenges and opportunities for implementing the new OIE biosafety standard in low resource settings"

- A much stronger emphasis on risk assessment will require the technical resource to complete and to define controls for local or regional implementation
- Defining the local biosafety priorities
- Defining alternative controls in the absence of data
- Setting acceptable targets for the residual risk from work with biological agents
- Developing "template biorisk management systems" for typical functional laboratory groups to provide the technical guidance that is needed for alternative safety systems

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Case Study

Quantitative Risk Management for high consequence biological risks

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Piper Alpha

An explosion and resulting fire destroyed the platform on July 6, 1988, killing 167 men.

“Piper Alpha must never happen again”

The Cullen Report - Offshore Safety Case

- Safety Case Process 1993
- Goal Setting Approach
- 75% reduction in incidents off-shore

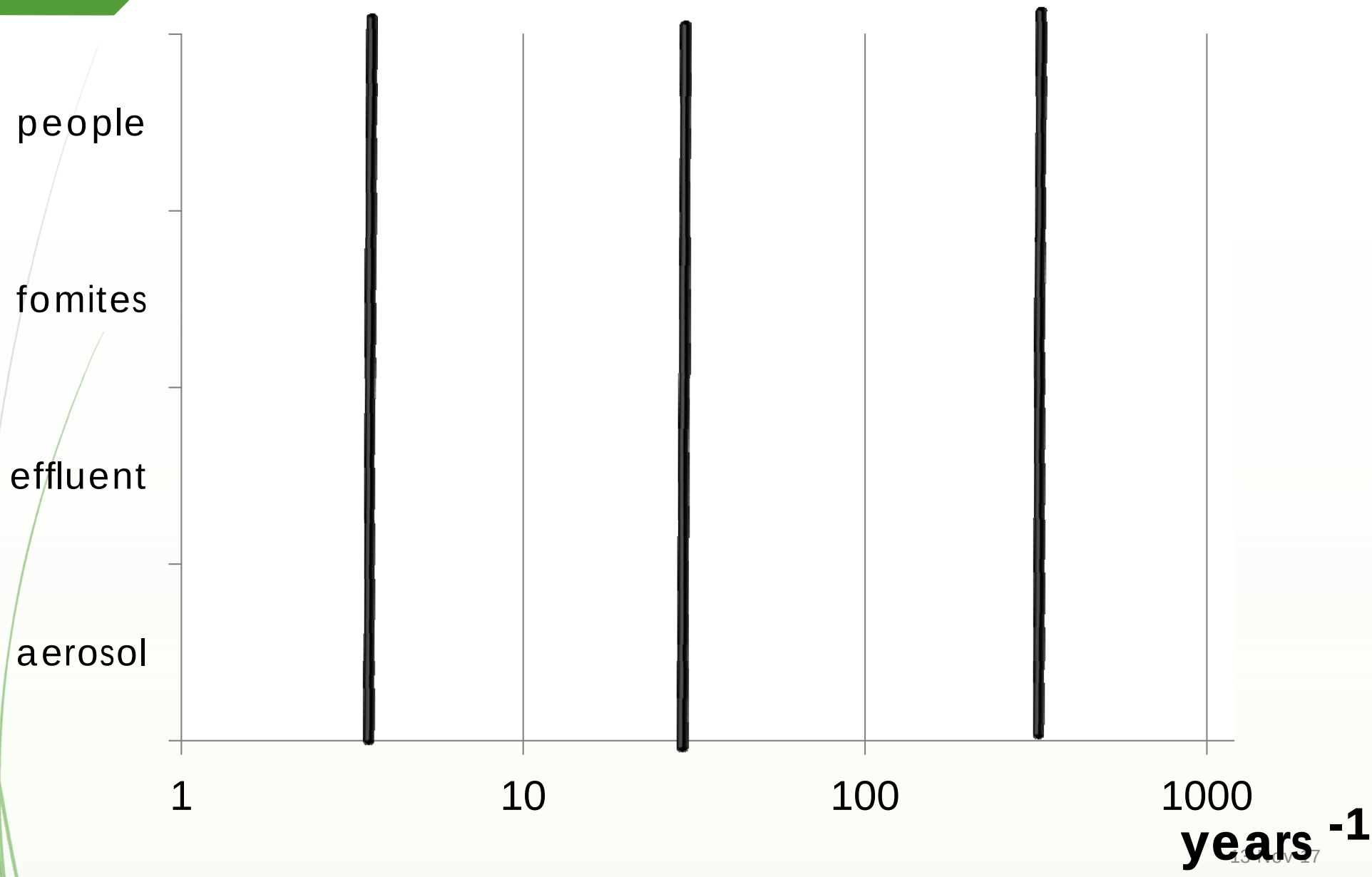
http://www.hse.gov.uk/offshore/safetycases.htm

Piper Alpha and FMDV

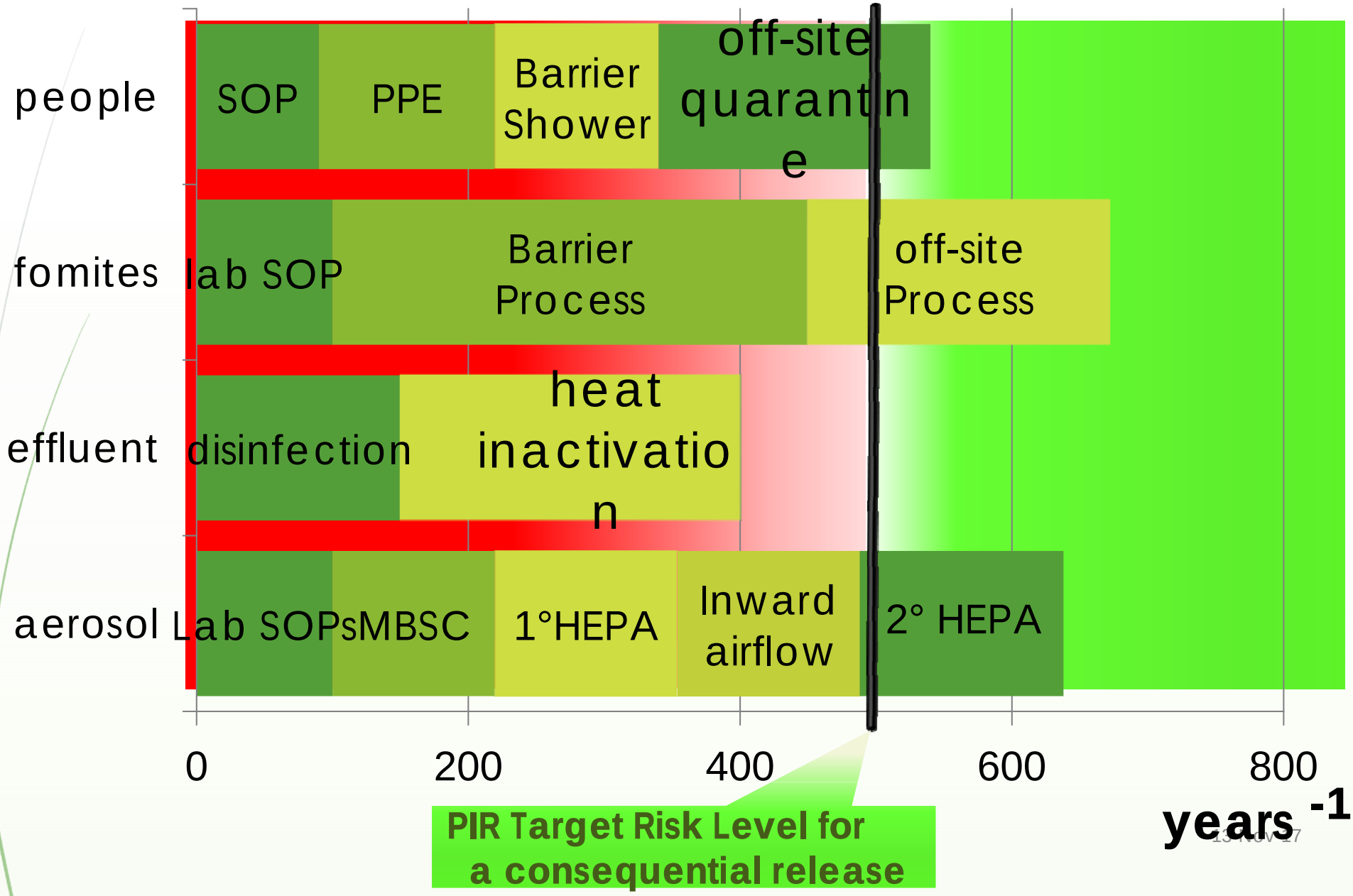
- 167 deaths in 22 minutes
- >3.4 billion GBP
- Safety Case regime in 1993
- IEC61508 philosophy

- 2007 outbreak – 200 m GBP
- 2001 outbreak – 8 billion GBP
- No proven transmission chain
- HSE: FMDV facilities –> „high hazard industries“
- Change of the regulator
- IEC61508 philosophy

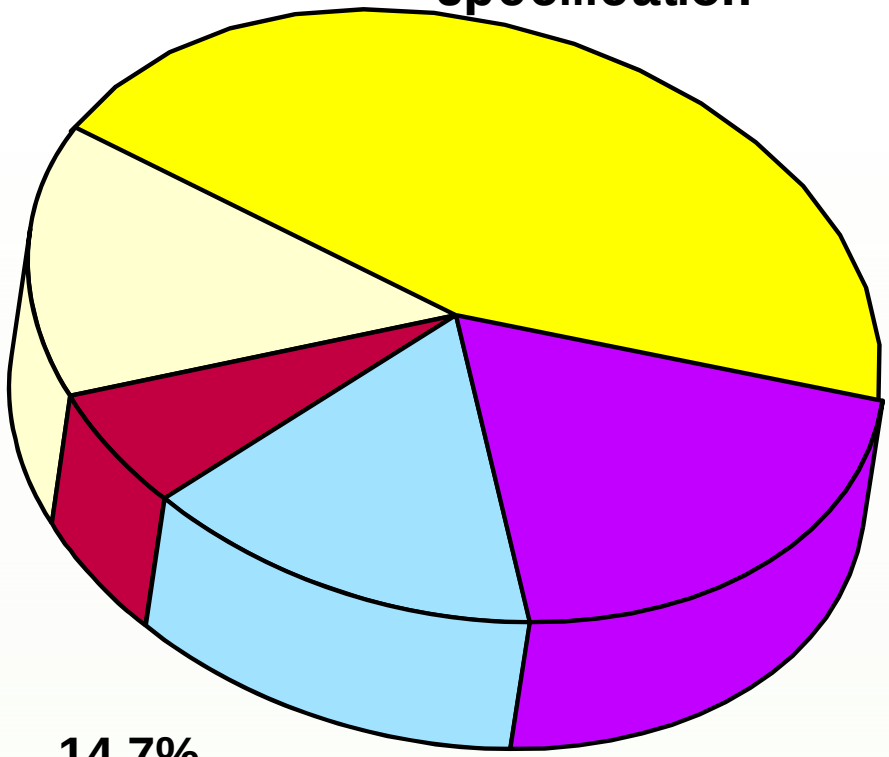
Target Risk Concept



Risk of consequential environmental release



Causes of safety system failures



More than 60% of failures "built into safety-related system" before taken into service

Courtesy HSE UK

ABSA, 60th Annual Biological Safety Conference
Albuquerque, New Mexico, 13-18 October, 2017

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Structured Risk Assessment and Risk Management –

The Biorisk Bowtie

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Risk Management

- Can everybody in your facility explain why (s)he has to apply which control and where?
- Are our risk assessments fit for purpose?
- Are they available to everybody?
- Are they kept upto date?
- Do they help us to optimize risk?

- Are they reproducible?
- What methodology to use?

Advancing Risk Assessment Approaches

A
Compliance

B
EU GM Assessments

C
High Hazard Industries

pro

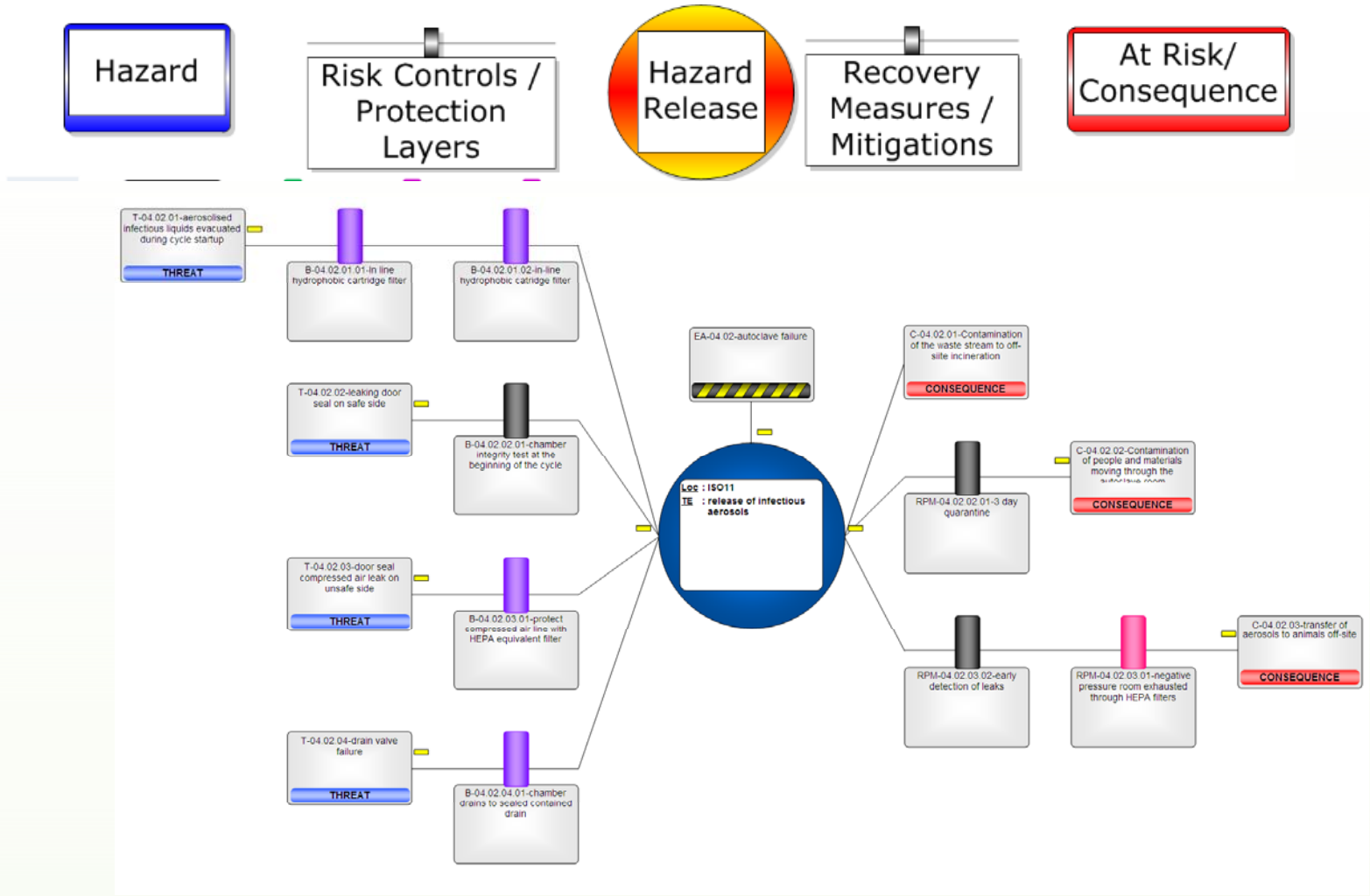
- Encourages solutions tailored to local settings
- A framework for conducting targeted risk assessments, setting out why and where controls are needed.
- Long term better risk management and lower total cost of ownership

con

- **High requirements for risk assessment resource to enable and justify different approaches for local controls**

Bowtie Risk Assessment Methodology

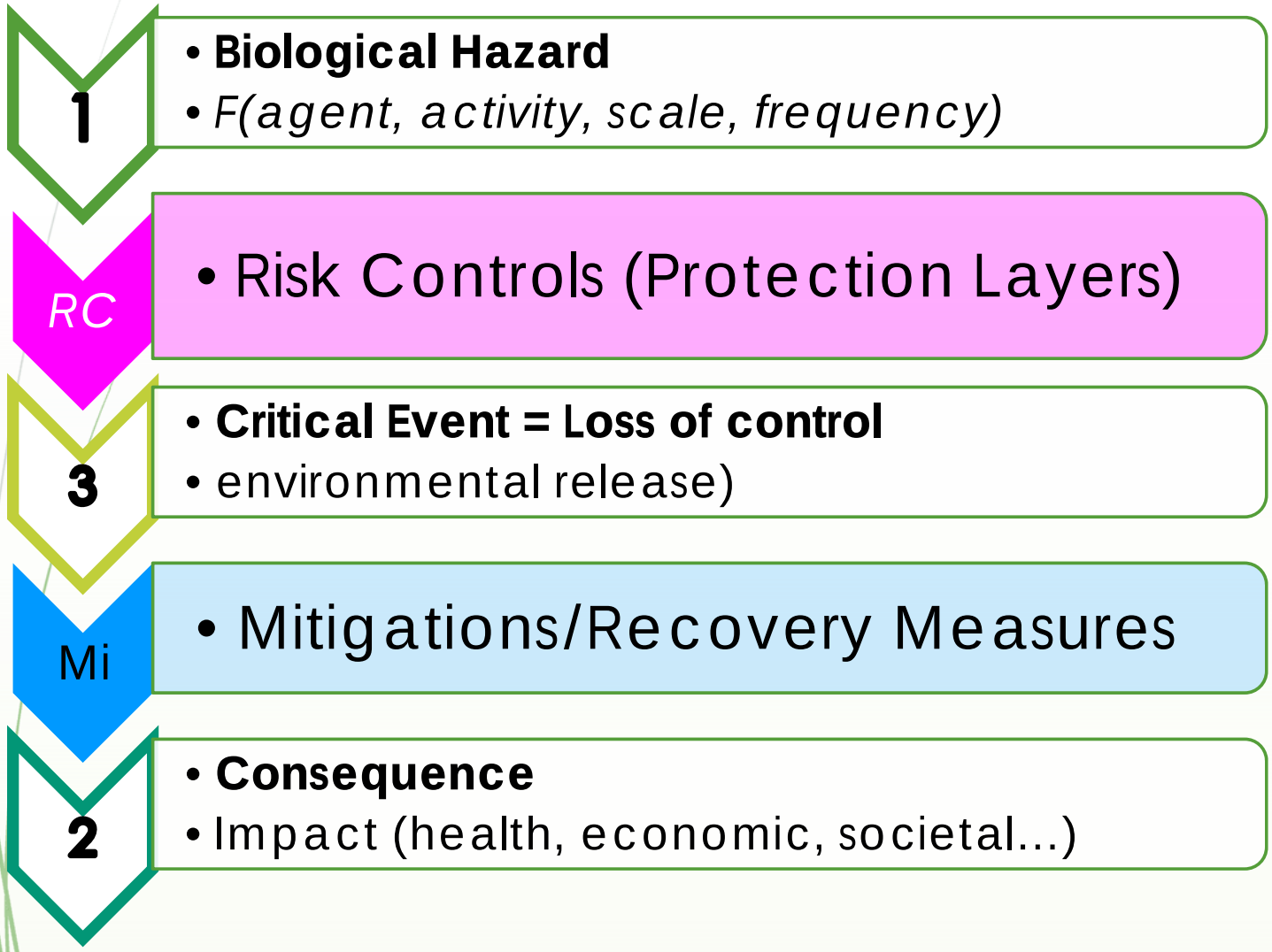
Source.....critical event.....receiver



Risk Assessment Process

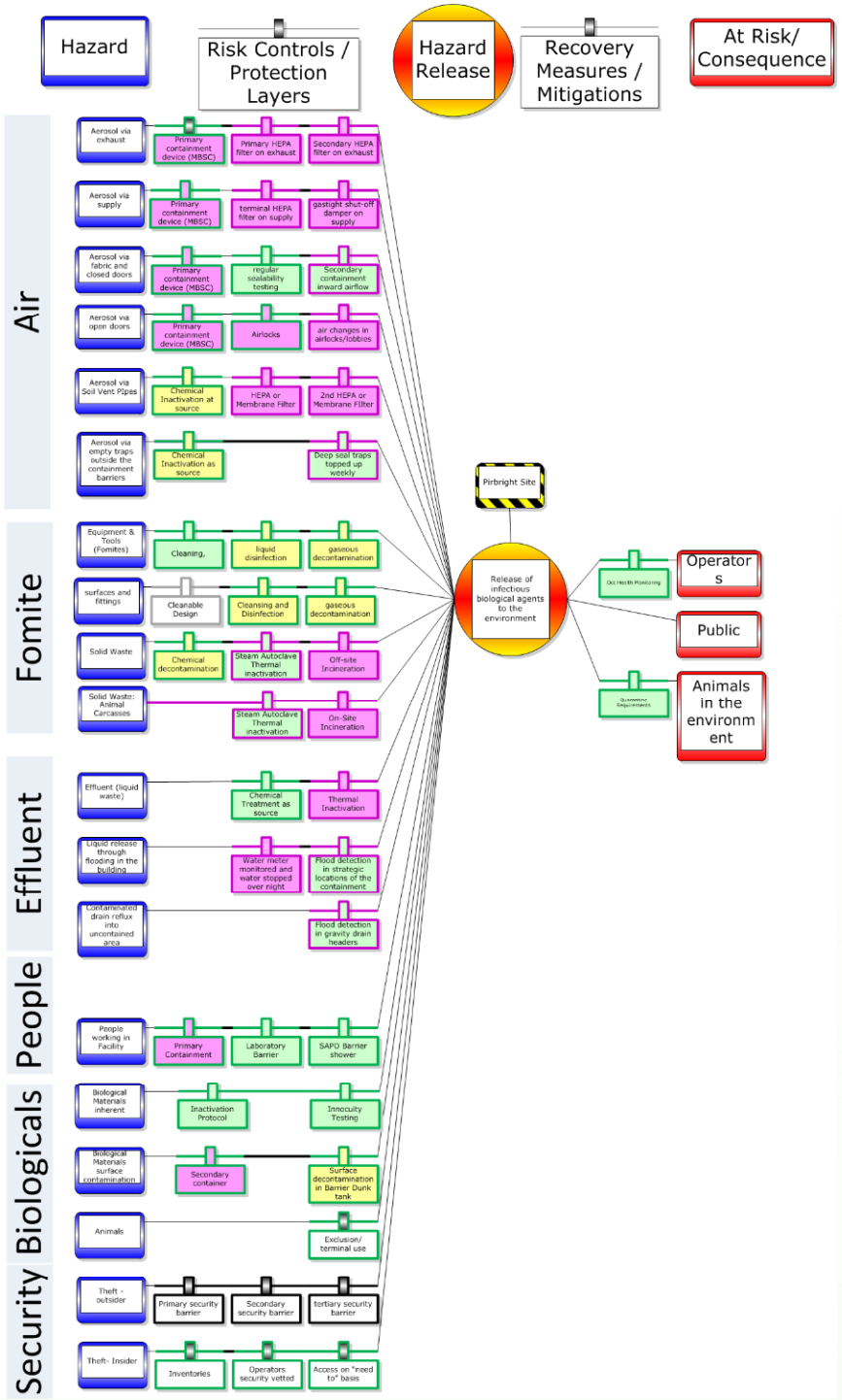
1. • **Biological Hazard**
   • *F(agent, activity, scale, frequency)*
2. • **Consequence**
   • Impact (health, economic, societal…)
3. • **Critical Event = Loss of control**
   • environmental release)

Risk Assessment Process



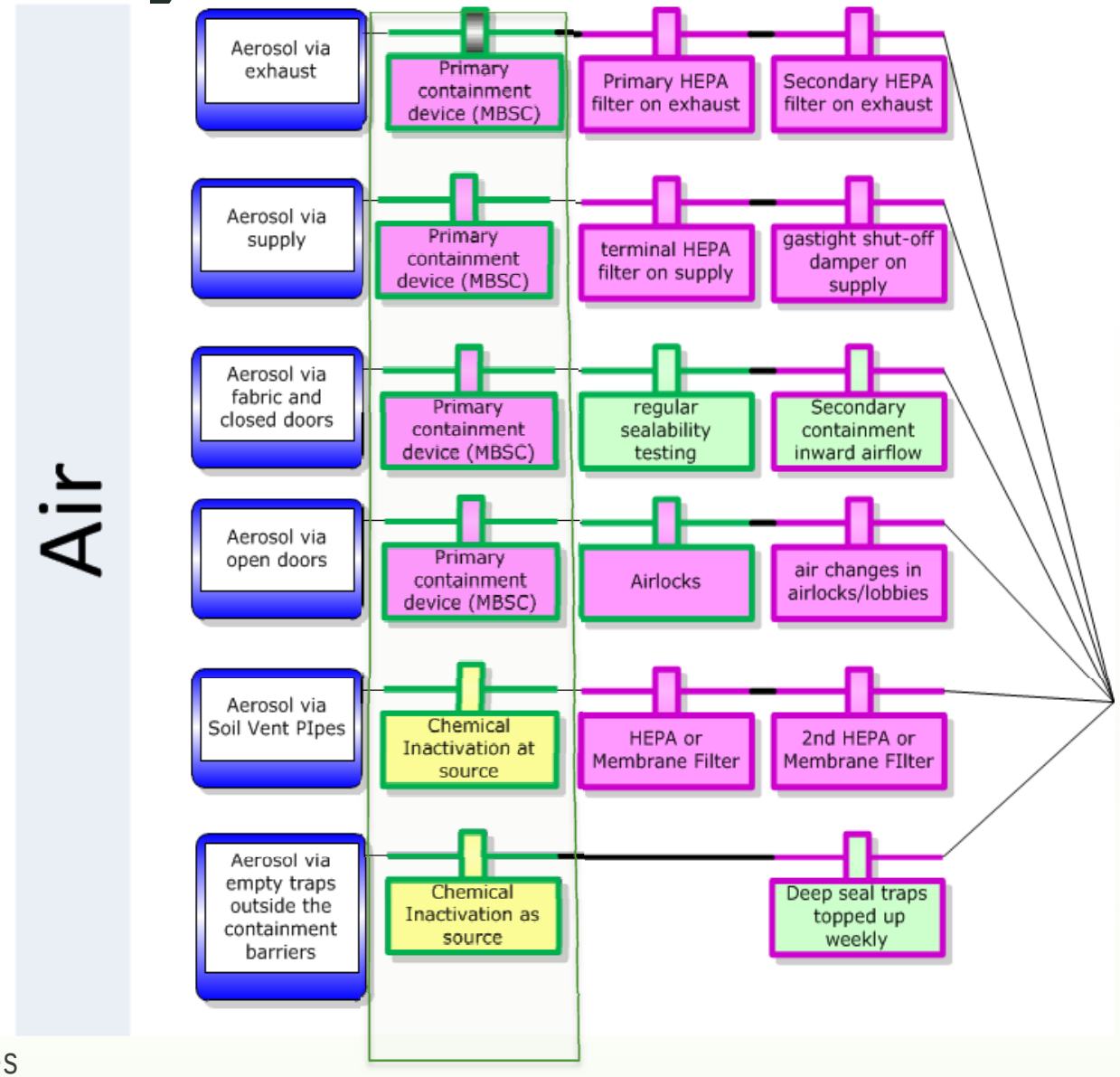
Environmental Risk Model

- Critical Event: Loss of environmental containment
- Risk Path Category
- Risk Path defined by biohazard, activity and escalation path
- Definition of



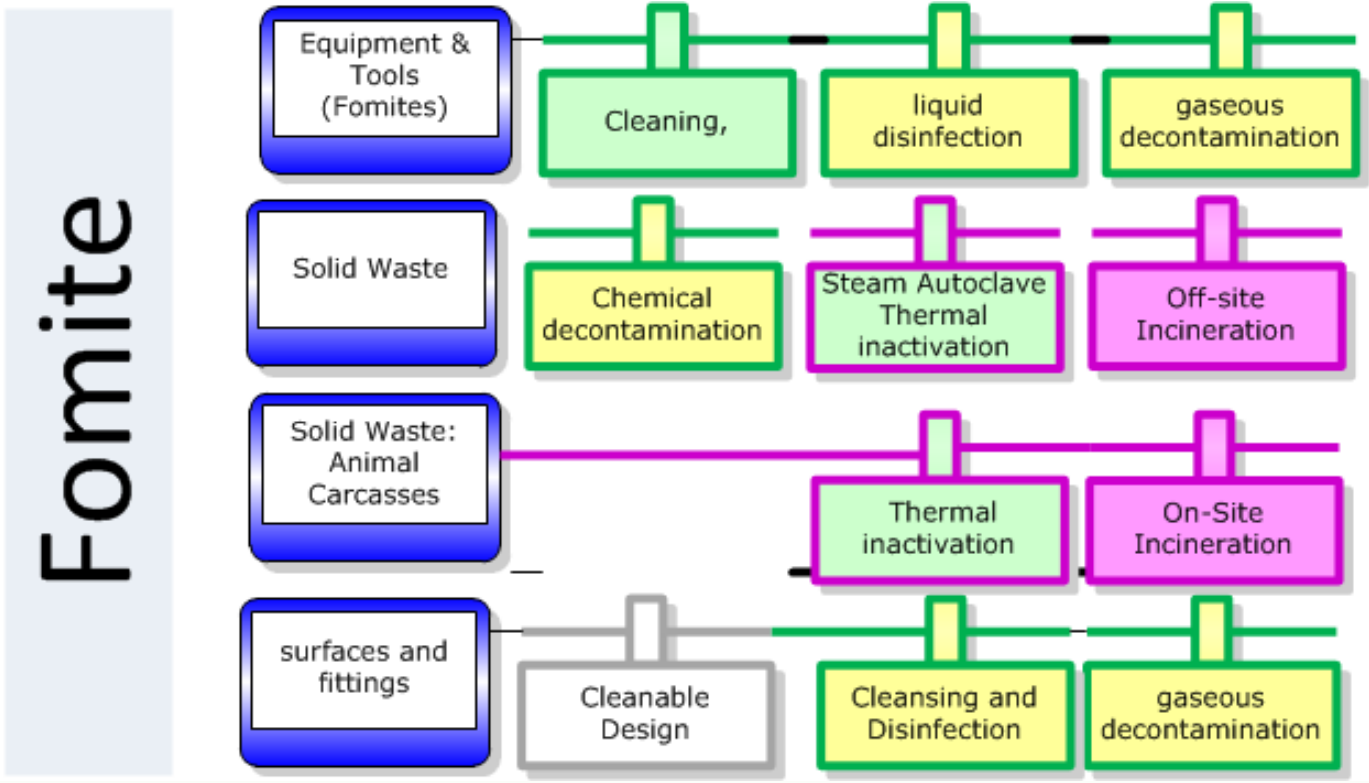
Risk Control Systems Air

1. Primary containment devi
2. HEPA filtration on extract
3. 2nd HEPA on extract and HEPA on supply
4. Deep seal traps
5. Soil vent filters
6. Airlocks
7. Inward directional airflow (pressure cascades)
8. Room Sealability for gase decontamination
9. Ability to isolate each spa on supply and exhaust
10. Air pre-filtration in primary containment spaces
11. Air changes in laboratories
12. Laminar airflow



Risk Control Systems – Fomites & Solid Waste

1. Cleaning
2. Disinfection
3. Gaseous decontamination
4. Steam Autoclave
5. Dunk Tank
6. On/off- site incineration
7. (natural inactivation)



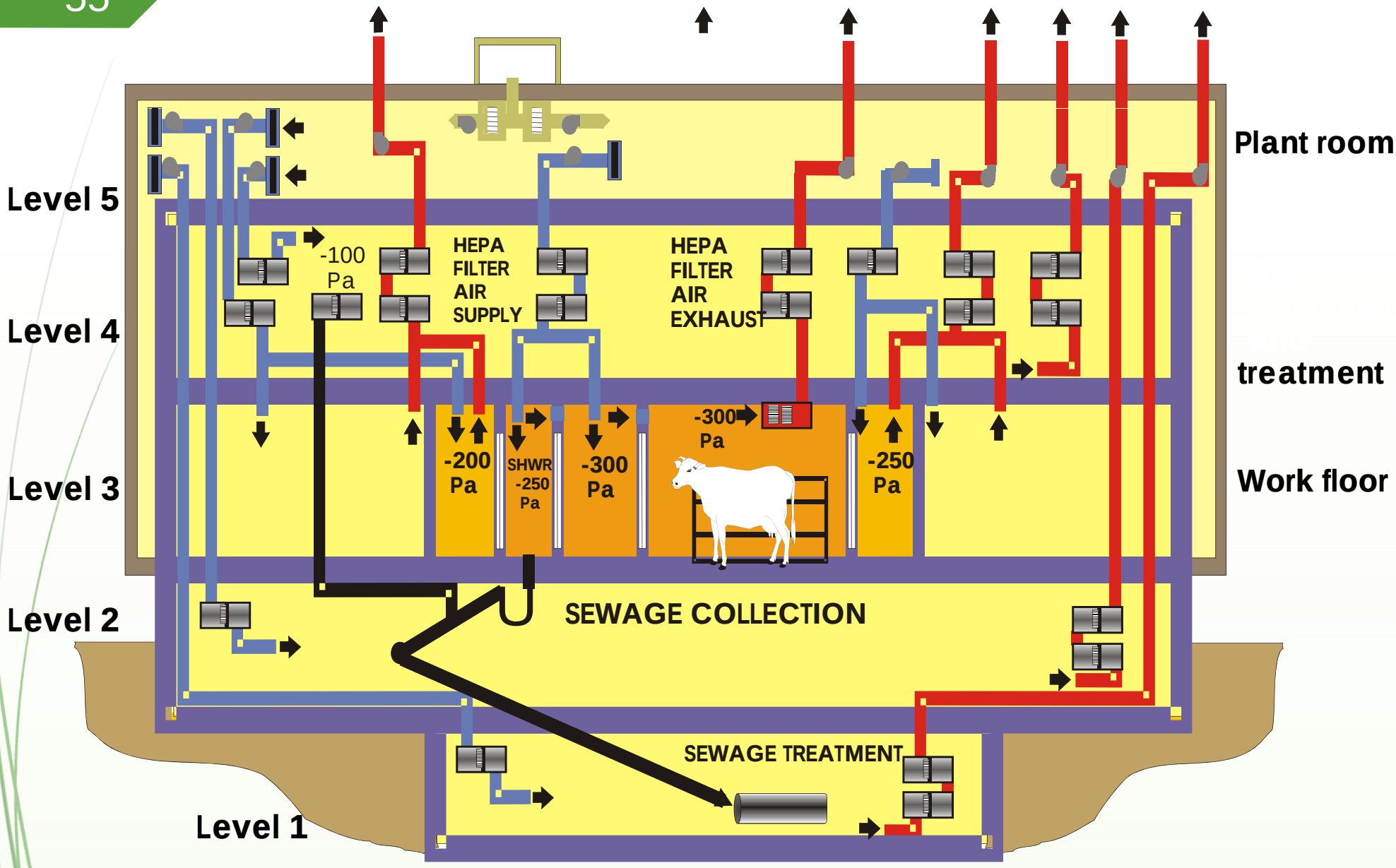
During operation fomites can be any inanimate object that is removed from the containment, including waste. During shut-down and with respect to operator exposure the ability to decontaminate fabric, fixtures and fittings is equally important

Controls – Protection Layers

Passive Controls	Dynamic Controls	Management Controls
air tight barrier construction	directional inward air flow	Alarm Response Protocol
Double Exhaust HEPA filtration, supply HEPA protection	Air changes Open door velocity air flow	HEPA filter validation
Compression seal door	Inflatable seal door	Protective Clothing
Multiple compartment access lobbies	Barrier shower & change protocols	Process validation
Box in a box principle	Fully encapsulated suits ?	Procedures

- risk path consequence
- risk path likelihood
- detectability of failure

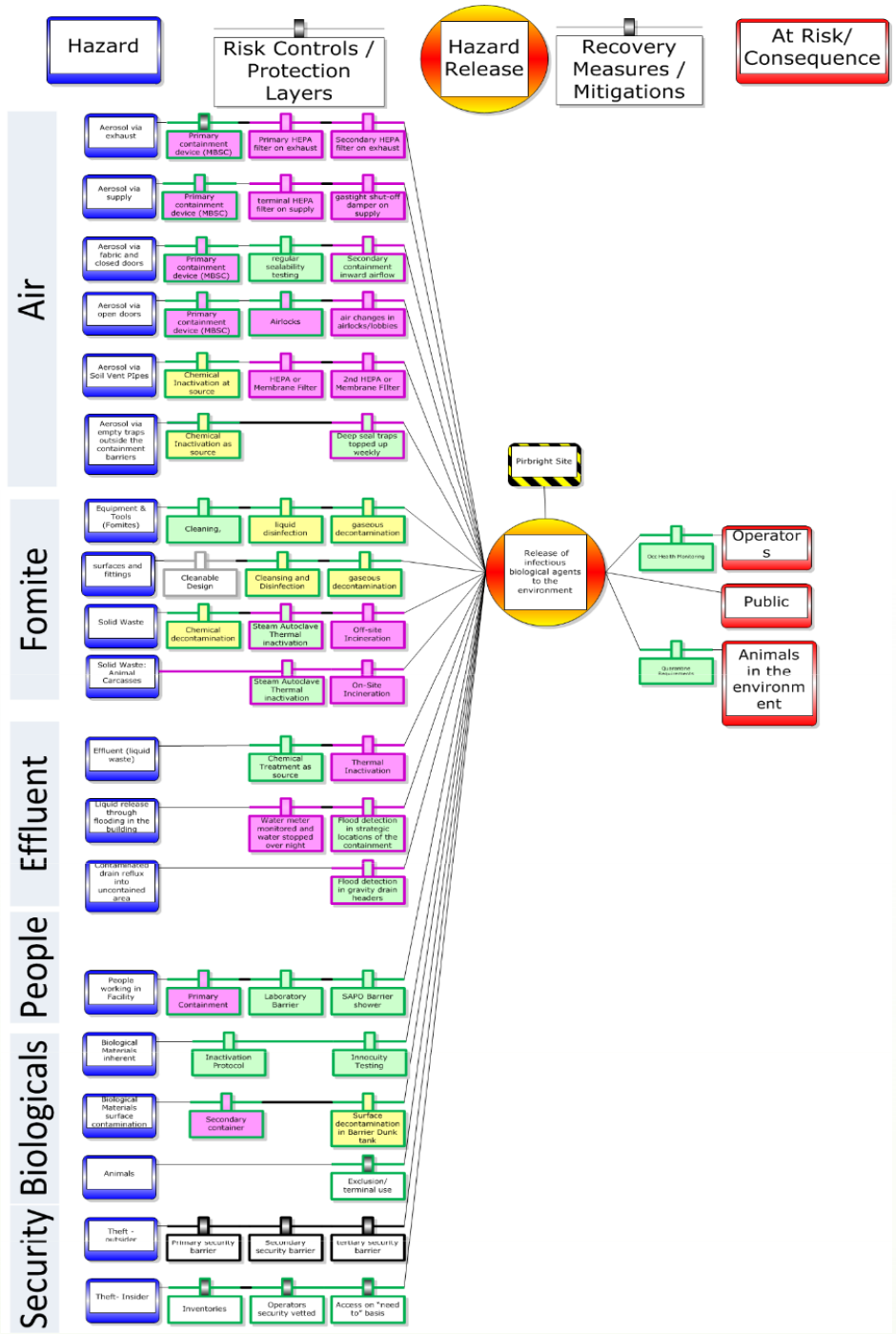
BIOCONTAINMENT AT AAHL



courtesy Australian Animal Health Laboratory

Conclusions

- Application of the new process must focus on meeting the needs of all stakeholder, including those who receive downstream materials from a facility
- To enable trust between countries, it is necessary to better characterise the performance of alternative and conventional controls
- For suitable biorisk management setups in **any** resource settings good training in risk assessment is essential



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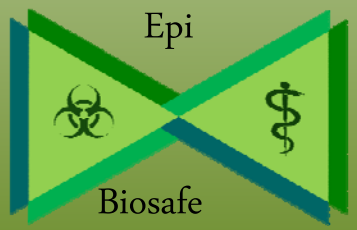
Concept

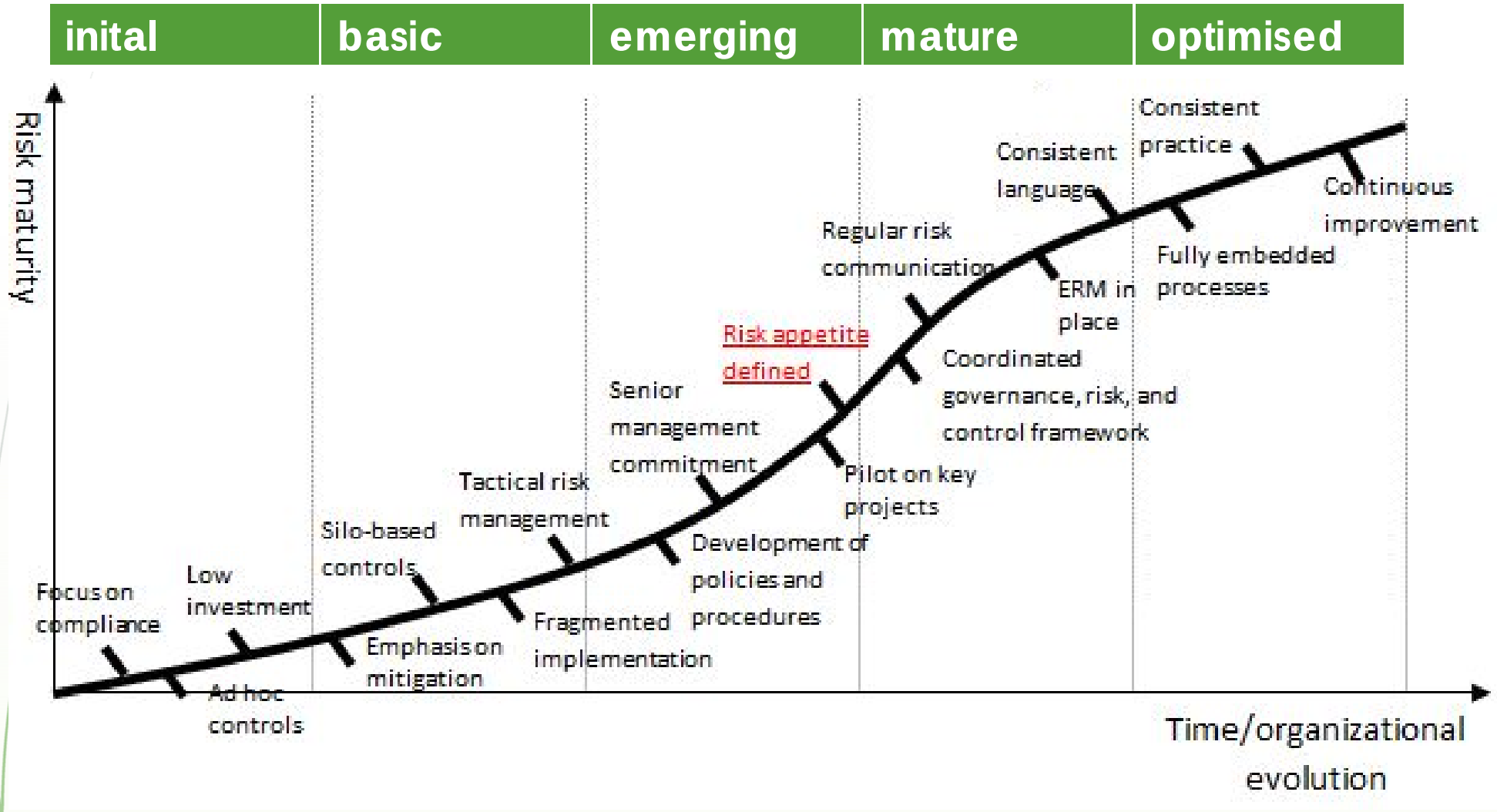
Risk Management Maturity - Compliance versus Performance



Risk Managment Culture Components

source: The Institute of Risk Management

A journey towards a mature biological risk management system



Source: Chartered Institute of Internal Auditors
https://www.iia.org.uk/resources/risk-management/risk-appetite/

Conclusion

- Moving organisations to excellence in biological risk management is a journey.
- Compliance without risk ownership and risk management provides a false sense of security
- Managing high consequence pathogens requires complex facilities, which require a **mature risk management culture**
- **High Reliability Organisations** thrive on excellence in risk management to stay **compliant, safe,** and **sustainable**

Conclusion

To achieve the goals of sustainability and reliability in biological risk management we have to counter the expectation that biosafety is an on/off state and promote that good risk optimisation based on data and good process will yield more benefits to the society and

Compliance should be a natural by-product of good risk management.

Acknowledgement

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Note: This presentation is not expressing the opinions of Merck or MSD.

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The Elizabeth R Griffin Research Foundation
http://www.ergriffinresearch.org/

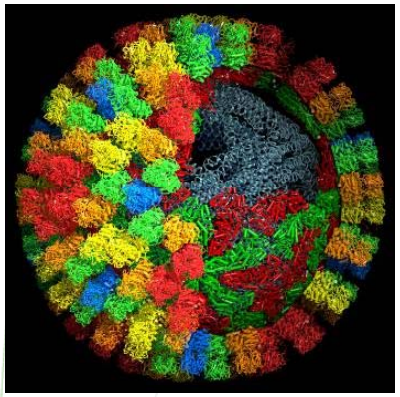
EUFMD Biorisk Committee
European Commission for the Control of Foot and Mouth Disease

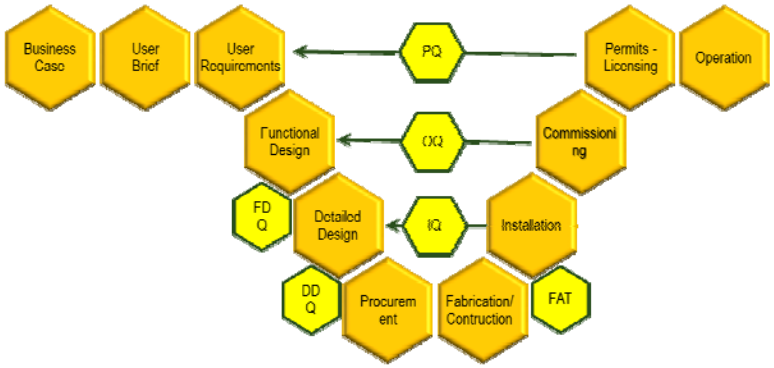
International Veterinary Biosafety Workgroup
www.ivbw.camp9.org

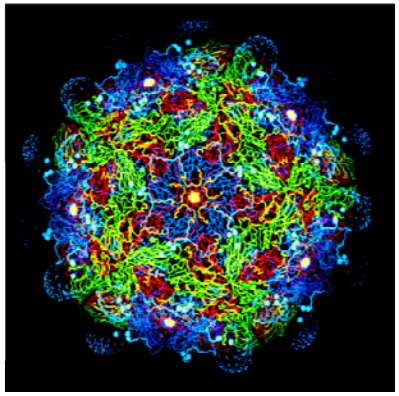
OIE ad hoc group for biosafety

European Biosafety Association
www.ebsaweb.eu

Epibiosafe
www.epibiosafe.com







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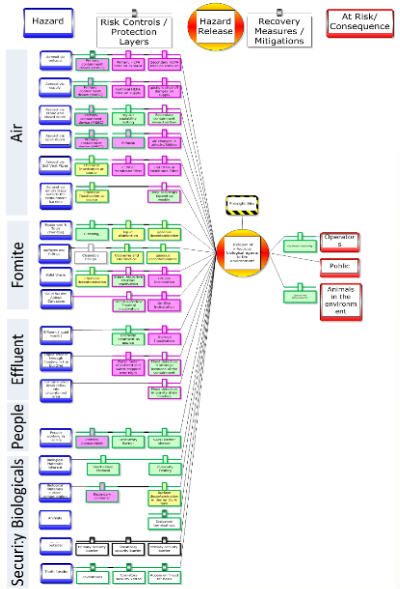

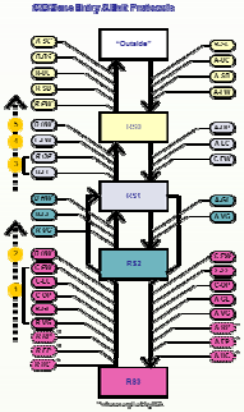

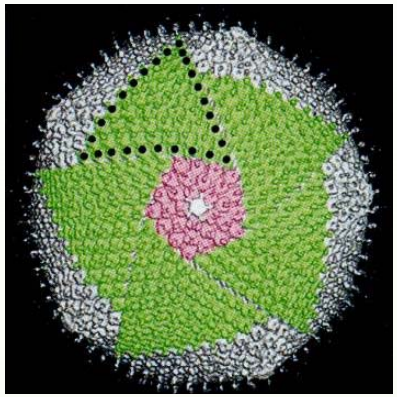

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