The New FMD Containment Zone Proposal and Vaccination.

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Topics for todays presentation.

1. Current and proposed containment zone concept

2. When to use limited vaccination and how zones might be used in high density areas

3. Risk based decision-making for vaccine banks.

Canada is an FMD free country without vaccination and if Canada were to experience a FMD outbreak, the desired outcome is to re-establish FMD-freedom without vaccination as quickly as possible.

- Currently best estimates put this time at between 12 and 18 months

- Can this time frame be reduced for the whole country or perhaps a portion of it and how might this be done?

Recovery of freedom

- On confirmation of a case of FMD in a free country, the status of the whole country is suspended.
- Return to trade is a two step process.
- Country freedom must be first be reinstated by the OIE and then the trading partners must negotiate a return to trade.
- The OIE sets out in Article 8.8.7 the conditions for recovery of freedom.
- If the Scientific Commission believes that the dossier submitted to them by a country has satisfied those conditions, they may reinstate a countries free status.

Recovery of freedom

- Reinstatement of that status does not automatically mean normal trade will resume.
- Each trading partner will likely want to perform an independent evaluation of the measures that a country took to eradicate the disease in order to assure safe trade.
- The majority of the evaluation has to do with understanding response plans and the capability of the veterinary services to implement them.
- The USA and Canada decided, a number of years ago, that the majority of the disease status evaluation could be conducted in peacetime prior to an event occurring, and established a working group to perform country evaluations.

Zoning

- The process culminated in the 2012 signing the Regulatory Cooperation Council Zoning Arrangement, under which both countries would recognize each others free areas, outside of the areas under control, and resume trade from those free areas.
- CFIA and USDA-Aphis used this arrangement successfully in 2014-2015 during the Avian Influenza (AI) outbreaks on both sides of the border.
- Would this work for FMD?
- Unlike AI, FMD is a country freedom disease so a country cannot self declare zones.

Zoning

- The OIE currently allows one type of zone to be established for FMD Outbreaks

- The OIE only allows the establishment of a containment zone only for limited outbreaks and but only after 28 days have passed since the last detected case was stamped out.

- *no new cases have been found in the containment zone within a minimum of two incubation periods as defined in Article 8.8.1. after the application of a stamping-out policy to the last detected case;* (Article 8.8.6. 6.))

Zoning

- Quads countries developed and submitted a proposal to the OIE for a modified containment zone concept that could be established during outbreaks.

- OIE's comments on the proposed alternative containment zone were very positive and the concept has been incorporated into the current horizontal chapter on zoning and compartmentalization (Chapter 4.3).

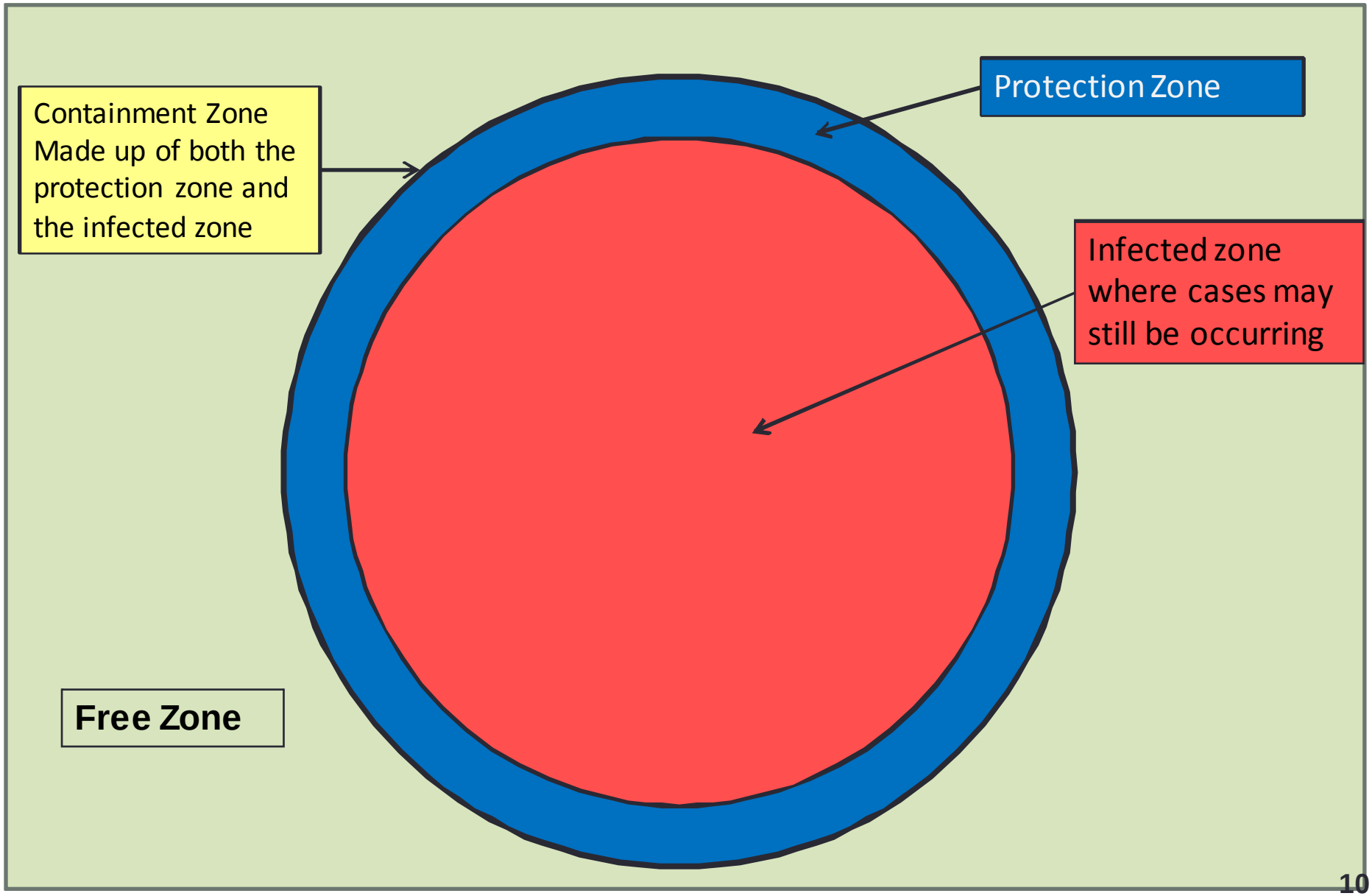
Zoning

- The term limited has been removed from the first sentence. (only for ~~limited~~ outbreaks)

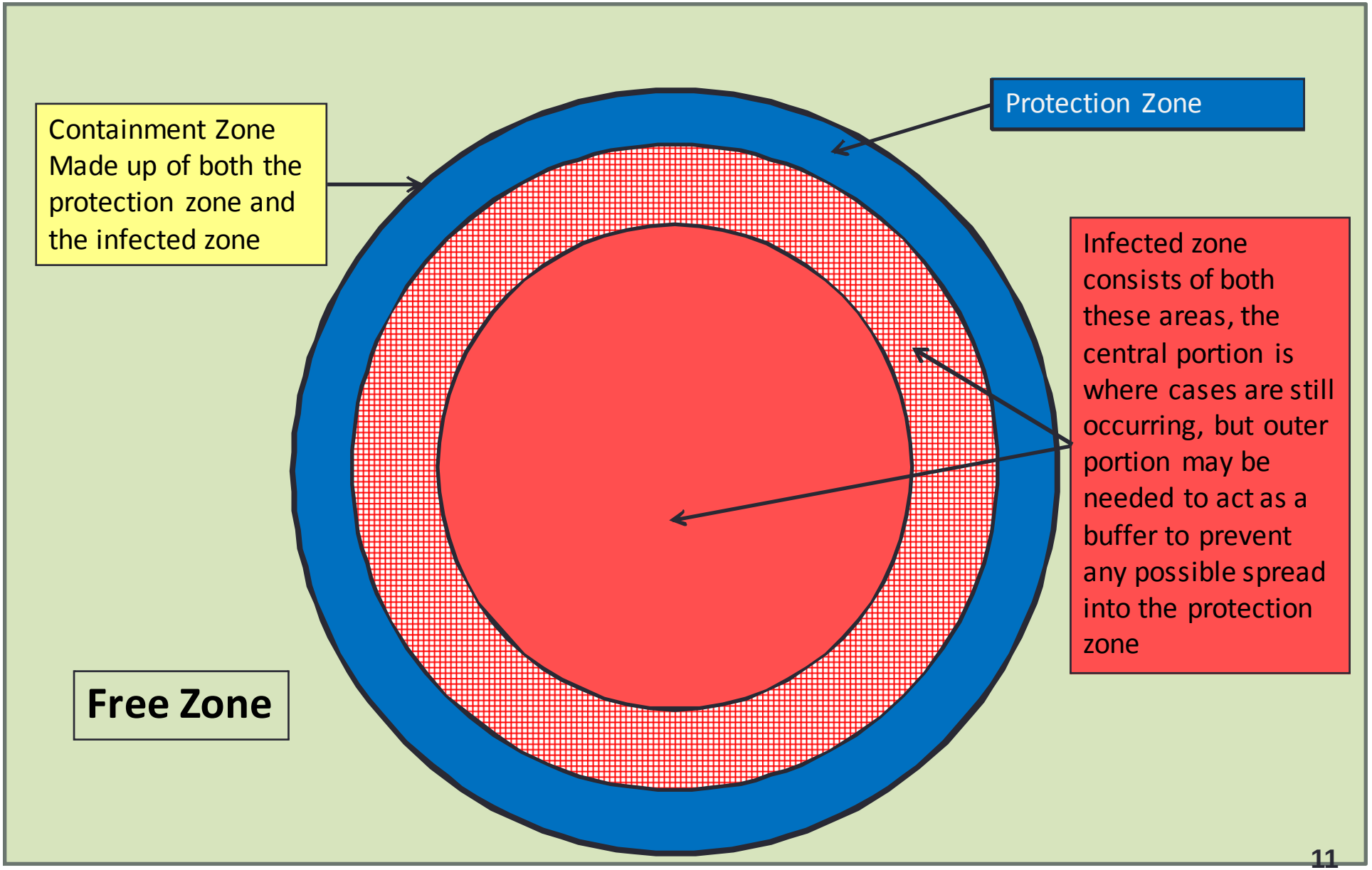
- In Chapter 4.3, Article 4.3.7 establishment of a containment zone now contains an either (the previous version of containment zone) or (the new concept)

- the *containment zone* comprises an *infected zone* where *cases* may continue to occur and a *protection zone*, where no *outbreaks* have occurred for at least two *incubation periods*, and that separates the *infected zone* from the rest of the country or *zone*.

Quads Containment Zone Proposal



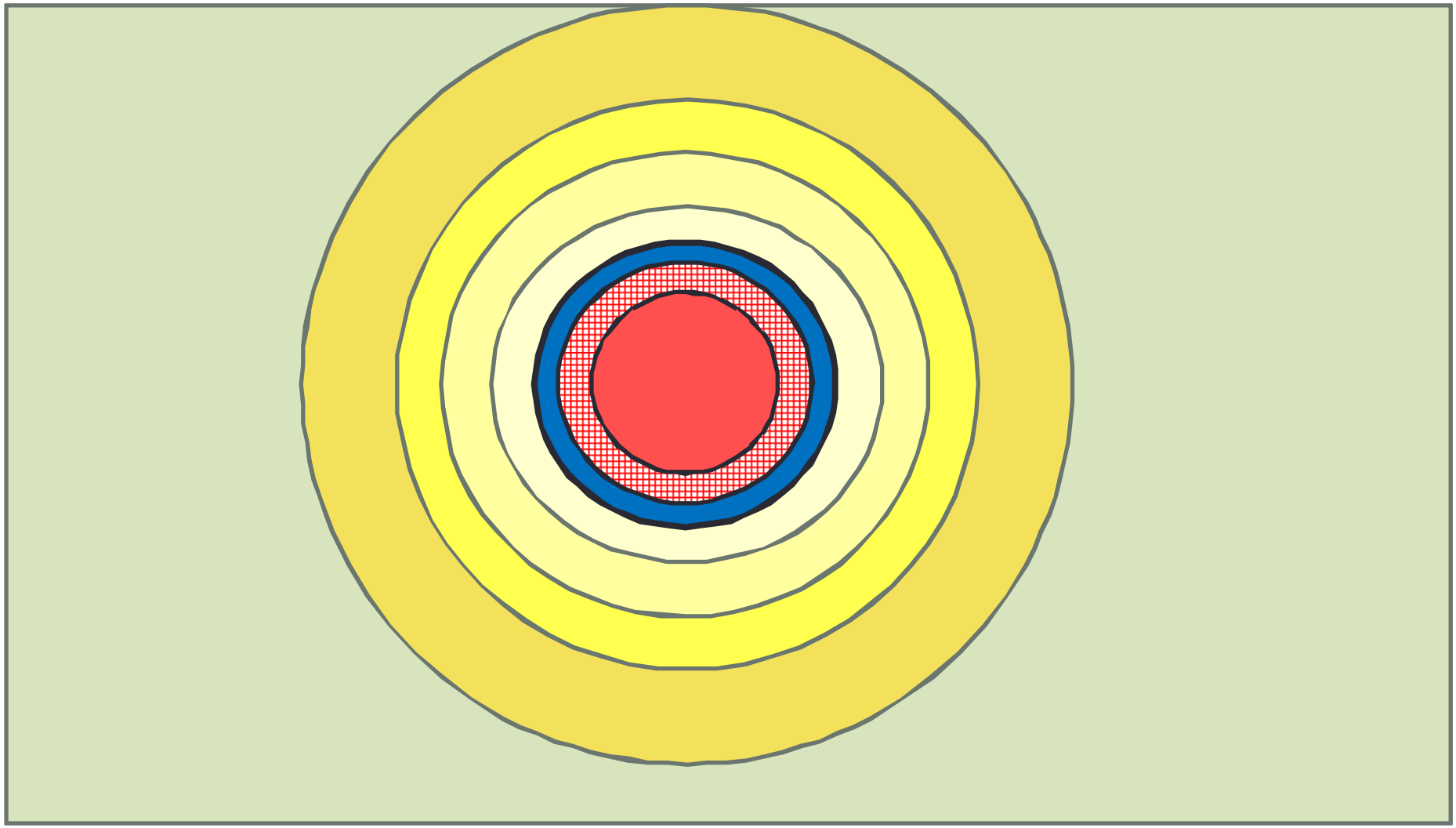
From a policy point of view, should the infected zone actually be split?



Establishment of the free zone

- A dossier documenting the control measures implemented and the surveillance conducted in the free zone will be required by the OIE for a decision to be made by the Scientific Committee to approve the zoning.
- Surveillance in the free area is key to providing the required proof of freedom.
- Needs to be done quickly. (28 days)
- What kind of surveillance is required.

Surveillance is required.



Surveillance is critical.

- Surveillance in a FMD free country without vaccination is not the same as in a FMD country free with vaccination and may be much more challenging depending on the amount of active surveillance being conducted.
- Clinical surveillance in FMD free countries without vaccination forms a large part of countries claim to freedom.
- Could you augment that with some serological surveillance?
- What about PCR on bulk milk tanks or saliva samples taken from feed?
- Would countries that are FMD free with vaccination have to rely solely on serological surveillance? Can they include any active surveillance? What form would that surveillance take?

Surveillance is critical.

- The Quads countries have a project underway to look at how we provide proof of freedom quickly for the area outside the containment zone.
- We are also developing a high throughput PCR for use on bulk tanks that can be used to blitz large areas. Canada, USA, UK and Australia.
- Zoning may not be able to be used in all cases, but it adds another tool to our toolbox.
- Zone size needs to include all outbreaks and therefore could be very large.

Vaccination Modelling

- When should vaccination be used?
- Does it reduce the length of the outbreak and the number of infected premises?
- Can we predict which outbreaks will be large?
- Is there a better way of dealing with large feedlots, instead of just stamping out?
- Would the ability to zone allow us to better make use of vaccination?

Use of vaccination during depopulation delays

- Most FMD eradication strategies call for killing of all animals on an infected farms within 48 hours.
- A consulting company, E-biz, recently reported to the Livestock Market Interruption Strategy Group that it would take approximately 78 days to depopulate a 25,000 cow feedlot. How many can be vaccinated per day?
- The animals would have all recovered from FMD by then.

Feedlots	Crew Size	Head/Hr.	Time Calcs	Time to clear 30%		Time to clear 100%	
Feedlot Size:				Low	High	Low	High
Over 15,000 Head (Use 25,000)	21	40	Hours	112.5	187.5	625	625
			Days (@8 hr)	14.1	23.4	78.1	78.1

Use of vaccination during depopulation delays

- This delay in depopulation increases the potential for virus spread.
- Can we increase the speed of depopulation or do we need an alternative.
- Farm staff could vaccinate 3 to 4 thousand animals per day. (CFIA oversight)
- Virus shedding is reduced 4 days after vaccination.
- All animals would be recovered in 14 days.
- Could we then send them to one of our slaughter plants to be culled.

Use of Zoning for Vaccination

- Vaccination causes delays in the return to freedom and trade.
- Could that delay in recovery of freedom be mitigated by holding all the vaccinates in a containment zone so that the area outside the containment zone could have its status re-instated as free without vaccination and then trade resume from that area.
- By having farm staff perform the vaccination, it frees up CFIA staff to do important diagnostic and surveillance work.
- Also depopulating at a slaughter plant frees up CFIA staff and the public is more receptive to the normal activities performed at that plant.

Vaccination - What are the trade issues ?

- Who pays for their continued care until they are dealt with?
- Could the animal or animal product be identified and marketed within Canada or could it even be sold outside Canada?
- Does the animal or animal product really have to just go in the ground.

Return to freedom delays

World Organisation for Animal Health

- The OIE code says that allowing vaccinates to live delays the return to freedom, 6 months vs 3 months.
- The Quads has been lobbying the OIE to harmonize the waiting periods, and an attempt was made two years ago, that a country using vaccinate to live, could return to freedom in 3 months if they conducted census surveillance of all vaccinates and their offspring.
- Census surveillance can not start until one month after disposal of the last animal depopulated. The reactors would have to be dealt with and a final report submitted to the OIE 2 months later.
- Would only work for small outbreaks.

Vaccination to help control large outbreaks

- Vaccination probably should be used if there are delays in depopulation as occurred in Japan where the average days to depopulation rose to 11.
- Is vaccination useful in large outbreaks as well?
- The Quads leads tasking the Quads Epi Modelling group, at a meeting in Victoria, British Columbia in 2012, with looking at how and when vaccination should be employed.

Quads Modelling

- The Quads Epi Modelling group plus the UK and the Netherlands, began a study on the use of vaccination in FMD using a multi-model comparison approach to compare different vaccination strategies in a FMD outbreak based on the UK's 2010 FMD simulation exercise, 'Exercise Silver Birch
- Exercise Silver Birch was chosen as it provided a plausible multi-focal outbreak with ready-to-use data.
- Each model was set up and parameterized to represent the scenario.
- Parameter input values for all models reflected the UK settings and FMD contingency plans to ensure consistency between models and their outputs.

Quads Modelling

- The key factors that were examined with respect to a vaccination programme included the vaccination approach (suppressive (SV) vs. protective (PV)), timing (when vaccination is carried out relative to the date of first detection), species to vaccinate, vaccination zone sizes, deployment methods, and resourcing.

- These factors were used to develop a series of 12 control strategies suitable for each model's configuration and requirements.

Quads Modelling

VACC STRATEGY	APPROACH	Min Zone Size (km)	Max Zone Size (km)	TIMING	SPECIES	Retrospective vs Prospective	Region	Priority
Stamping out	NA	NA	NA	NA	All	NA	All regions	NA
0	SV	0	3	14	All	P	All regions	Random
1	SV	0	3	14	All	P	All regions	Outside in
2	SV		3	14	All	P	All regions	Large farm size priority
3	SV	0	3	14	All	R	All regions	Outside in
4	SV	0	3	14	All	P	High risk regions only	Outside in
5	PV	5	10	14	All	P	All regions	Inside out
6	PV	5	10	14	All	P	All regions	Large farm size priority
7	PV	5	10	14	All	R	All regions	Inside out
8	PV	5	10	14	All	P	High risk regions only	Inside out
9	SV	0	3	7	All	P	All regions	Outside in
10	SV	0	3	28	All	P	All regions	Outside in
11	SV	0	1	14	All	P	All regions	Outside in
12	SV	0	5	14	All	P	All regions	Outside in
13	SV	0	3	14	Cattle only	P	All regions	Outside in

Quads Modelling

- The study showed that early vaccination can limit local disease spread around infected premises (IPs), and despite the delay in development of immunity, can be effective in helping to contain an outbreak.

- This is particularly the case when disease is widespread or fast spreading, or when authorities anticipate significant resource issues.

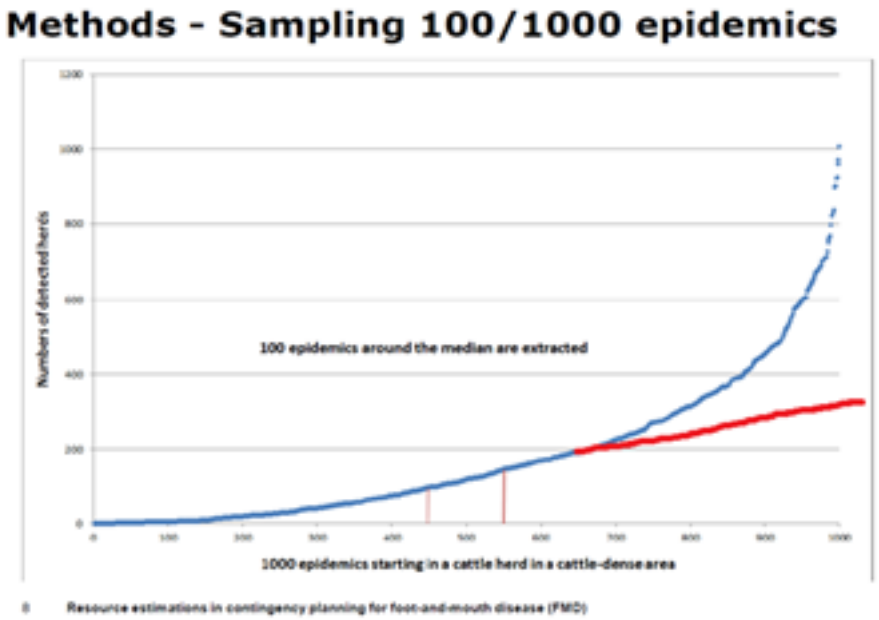
- Results of this study were published:
  - Roche SE, Garner MG, Sanson RL, Cook C, Birch C, Backer JA, Dubé C, Patyk KA, Stevenson MA, Yu Z, et al. *Evaluating vaccination strategies to control foot-and-mouth disease: a model comparison study*. Epidemiology and Infection 143, 1256–75, 2015

Quads Modelling

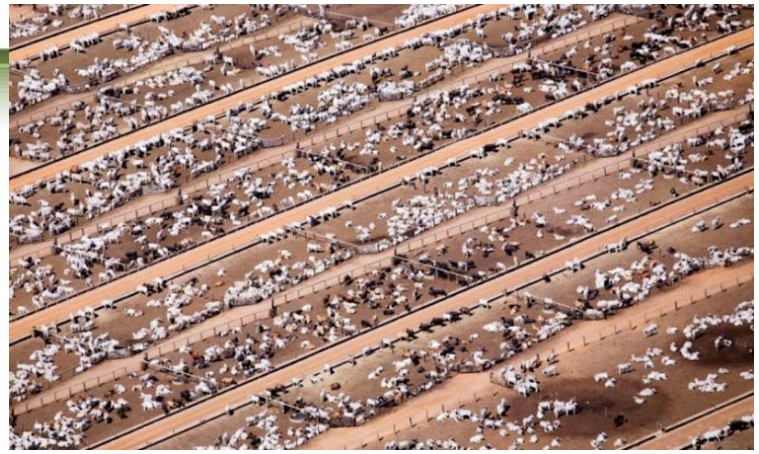
- But the study raised a number of questions.
- Were these results specific to the UK?
- Would the same results hold true when parameters, such as farm population data, introduction scenarios and stamping out policies specific to the other countries were used.
- Phase two of this project focused on assessing the robustness of particular vaccination strategies under different demographics and country specific settings

Vaccination to help control large outbreaks

- What our modelling studies showed was that even within specific countries, that use of vaccination in large outbreaks, reduced the length of the outbreak and the number of infected farms by almost half.
- Which outbreaks will be large??



Early decision indicators



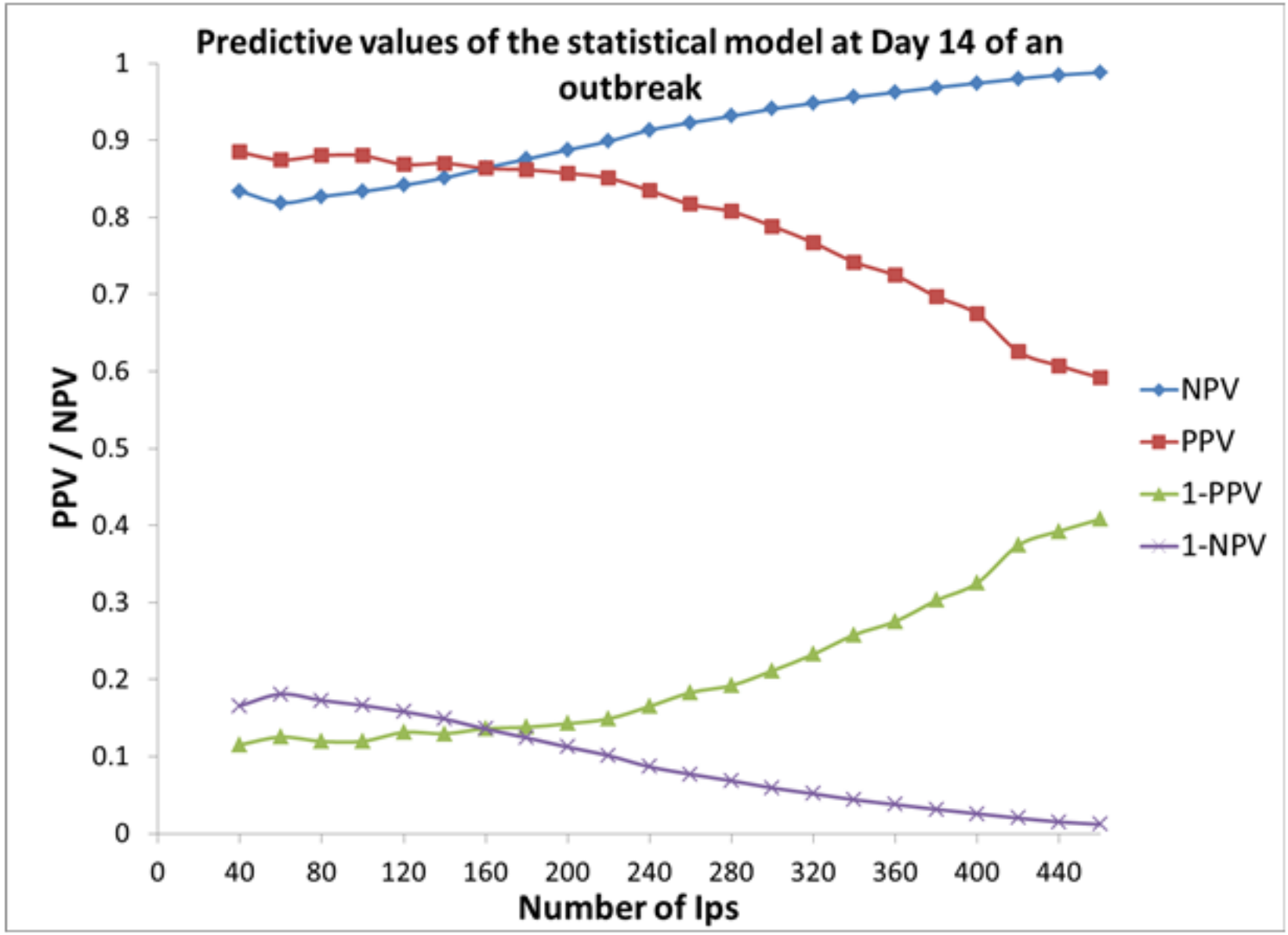
We are currently looking to see if Early Decision Indicators (EDI) can be used to predict large outbreaks. (54 outbreaks – 14 days)

		Actual outbreak size: Large	Actual outbreak size: Small	
Outbreak size as predicted by the model	Large	3673	538	4211
	Small	1000	4668	5668
		4673	5206	9879

Model predicted large outbreaks 4211 times, but 538 times it was small.
Error rate was 538 / 4211 = .1278

Model predicted small outbreak 5668 times but 1000 times it was large.
Error rate was 1000 / 5668 = .176

Early decision indicators



Do we have enough vaccine?

- The short answer is no!!
- Canada, Mexico and the USA are members of the North American Foot and Mouth Vaccine Bank (NAFMDVB) and contribute 10%, 20% and 70% to the funding of the bank respectively.
- We are currently moving storage of the VACs from Plum Island to Lyon France which allows us to have 2.5 million doses finished in 7 days.
- Most free countries that maintain banks also store at the manufacturers as well.
- **Vaccine Sharing Arrangement**. This arrangement allows us to leverage our supply to access additional doses without increased cost.
- VAC's that the NAFMDVB maintains are chosen on a risk based approach

Global FMD issues

- We are currently concerned with two main strains of FMD virus.
- O/ME-SA/Ind-2001 and A/ASIA/G-VII
- While O/ME-SA/Ind-2001 first appeared in Northern Africa in 2014, there have been multiple escapes from the Indian Sub-continent.
- The linage continues to spread with 2015-2016 introductions in UAE, Bahrain, Laos, Vietnam, Thailand, Mauritius and Myanmar.
- In November of 2016 there were 3 outbreaks in the Russian federation, close to the Chinese border and in South Korea which experienced 8 outbreaks in February of 2017.

Vaccine matching for O/ME-SA/Ind-2001

Sample	O 3039	O_1 Manisa	O/TUR/5/2009
ALG/3/2014	0.27	0.13	0.48
BAR/14/2015	0.32	0.13	0.44
BAR/8/2015	0.59	0.22	0.66
BHU/12/2012	0.17	0.12	0.23
BHU/1/2013	0.74	0.17	0.4
LAO/3/2015	0.52	0.18	0.72
LIB/1/2013	0.5	0.13	0.95
LIB/17/2013	0.19	0.12	0.38
LIB/22/2013	0.93	0.38	1.51
LIB/7/2013	0.51	0.16	0.91
MOR/1/2015	0.42	0.27	0.42
MOR/2/2015	0.55	0.32	0.58
MUR/6/2016	0.38	0.65	1
MUR/7/2016	0.35	0.76	0.87
NEP/13/2012	0.51	0.27	0.56
NEP/21/2012	0.24	0.12	0.46
NEP/6/2012	0.36	0.13	0.78
NEP/18/2013	0.4	0.2	0.63
NEP/6/2013	0.36	0.16	0.74
NEP/1/2014	0.37	0.16	0.35
NEP/6/2014	0.63	0.22	1.74
NEP/18/2015	0.54	0.27	0.59
NEP/11/2016	0.47	0.51	0.38
NEP/17/2016	0.41	0.68	0.89
SAU/1/2013	0.45	0.14	0.33
SAU/4/2013	0.63	0.15	0.54
SAU/6/2013	0.5	0.27	0.85
SAU/7/2013	0.54	0.32	1.15
SAU/1/2014	0.28	0.19	0.79
SAU/1/2016	0.89	0.39	0.89
SAU/7/2016	0.32	0.35	0.48
SRL/1/2013	0.46	0.23	0.76
SRL/1/2014	0.48	0.29	0.85
SRL/28/2014	0.58	0.25	0.42
SRL/30/2014	0.43	0.23	0.15
TUN/1/2014	0.26	0.11	0.52
UAE/1/2014	0.25	0.30	1.74
UAE/2/2014	0.42	0.27	1.1
UAE/1/2015	0.66	0.43	0.87
UAE/2/2016	0.55	0.34	0.55
VIT/8/2015	0.71	0.58	0.52
VIT/20/2016	0.66	0.56	0.66

42 field isolates

Using VNT r-value 0.3 cut-off

Not Matched	**r-value is <0.28**
Borderline	
Matched	**r-value is >0.32**

	Broad coverage: (ME-SA topotype)	O/PanAsia-2
Russian Suppliers	O-Manisa	O-Panasia2
Vetal, Turkey		O/TUR/07
Merial	O-Manisa	O-3039 (PanAsia-2 equiv.)
MSD	O-Manisa	O/TUR/5/09

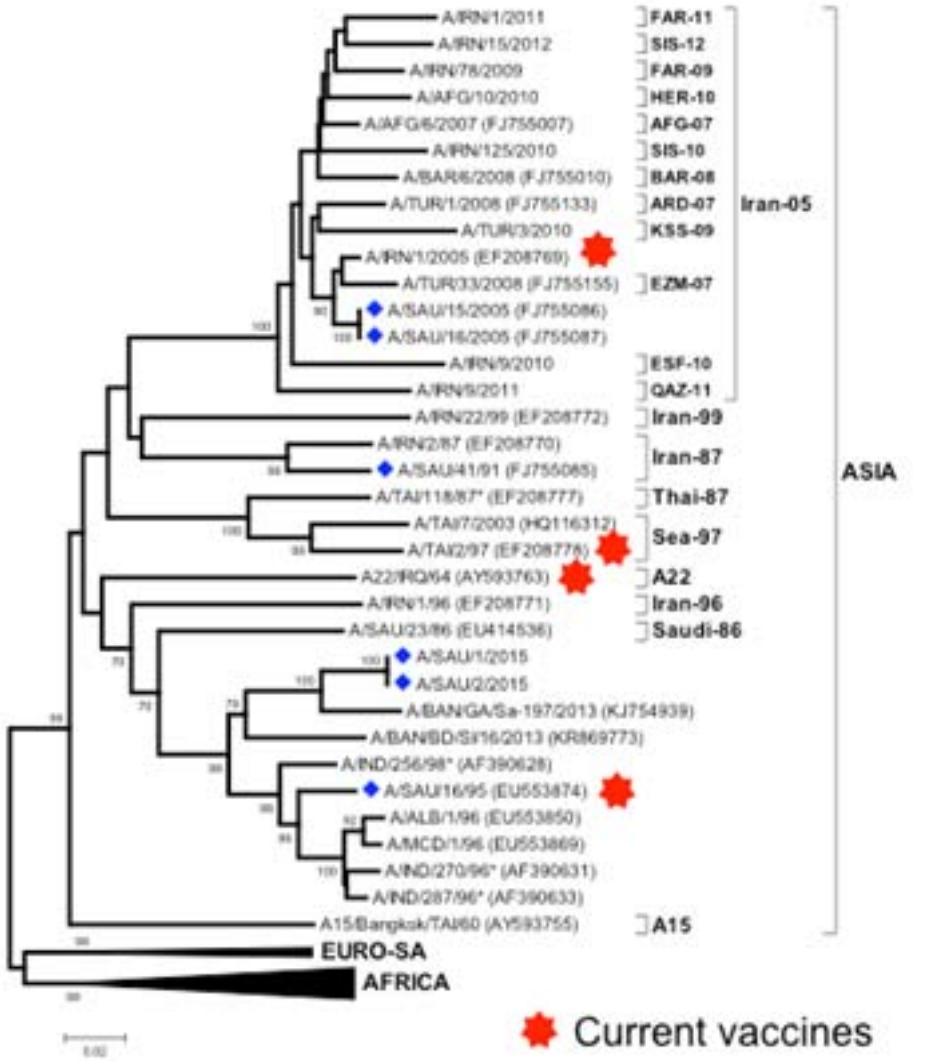
Global FMD issues

- Initial reports of A/ASIA/G-VII appeared in September of 2015 in Turkey, Saudi Arabia, Iran and Armenia.
- Again, this strain appears to have originated from the Indian sub-continent.
- Another example of a new unexpected FMD movement between the historic endemic pools.
- New cases in Turkey have been reported to be due to a new antigenic sub-lineage of A/ASIA/G-VII and they have deployed a new vaccine (Sam-16)
- Neither Merial or MSD currently have a vaccine that can cover this lineage – but new vaccines are expected sometime in 2017 in response to these outbreaks

A/ASIA/G-VII

Poor in-vitro match to many commercial vaccines

Recent r-values:	A/SAU/1/2015	A/SAU/2/2015	A/IRN/8/2015	A/IRN/12/2015
A-Iran-05	0	0	0	0
A-Iran-87	0	0.04	nd	nd
A-Iran-96	0.04	0.06	nd	nd
A-Iran-99	0.01	0.01	nd	nd
A-Sau-95*	0.20	0.19	0.26	0.16
A-22	0.11	0.11	nd	nd
A-Tur-20-06	0.03	0.06	0.01	0.15
A-May-97	0.14	0.23	0.15	0.23
A-Tur-11	0.01	nd	0.10	0.04
A-Tur-14	0	nd	0	0
A-IND-40-2000*	0.26	nd	0.03	0.24



* Multiple BVS tested

Conclusions

- Response to diseases such as FMD require a collaborative and innovative approach
- The CFIA is positioning itself to be able to respond more effectively in the event of a disease outbreak through the use of vaccination and zoning.
- We believe this will allow for more humane treatment of animals, faster containment of the disease, and a more rapid resumption of trade activities.

Questions / Preguntas ??