



The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) *Programa Integrado de Vigilancia de la Resistencia Antimicrobiana de Canadá*

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Epidemiólogo Veterinario

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Joint Biennial Meeting ReLAVRA-RILAA

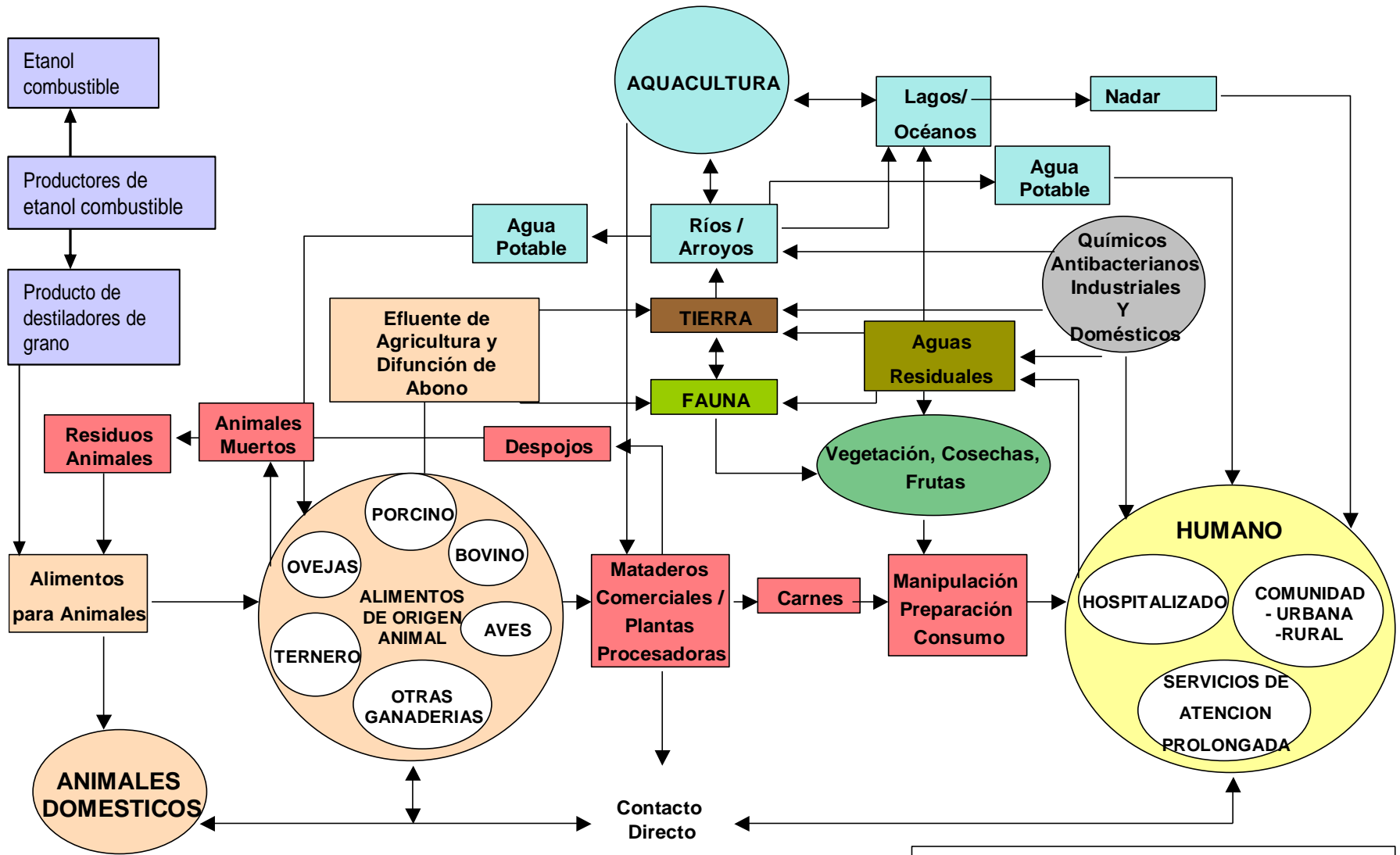
Montevideo

Uruguay

November 28-30 2017

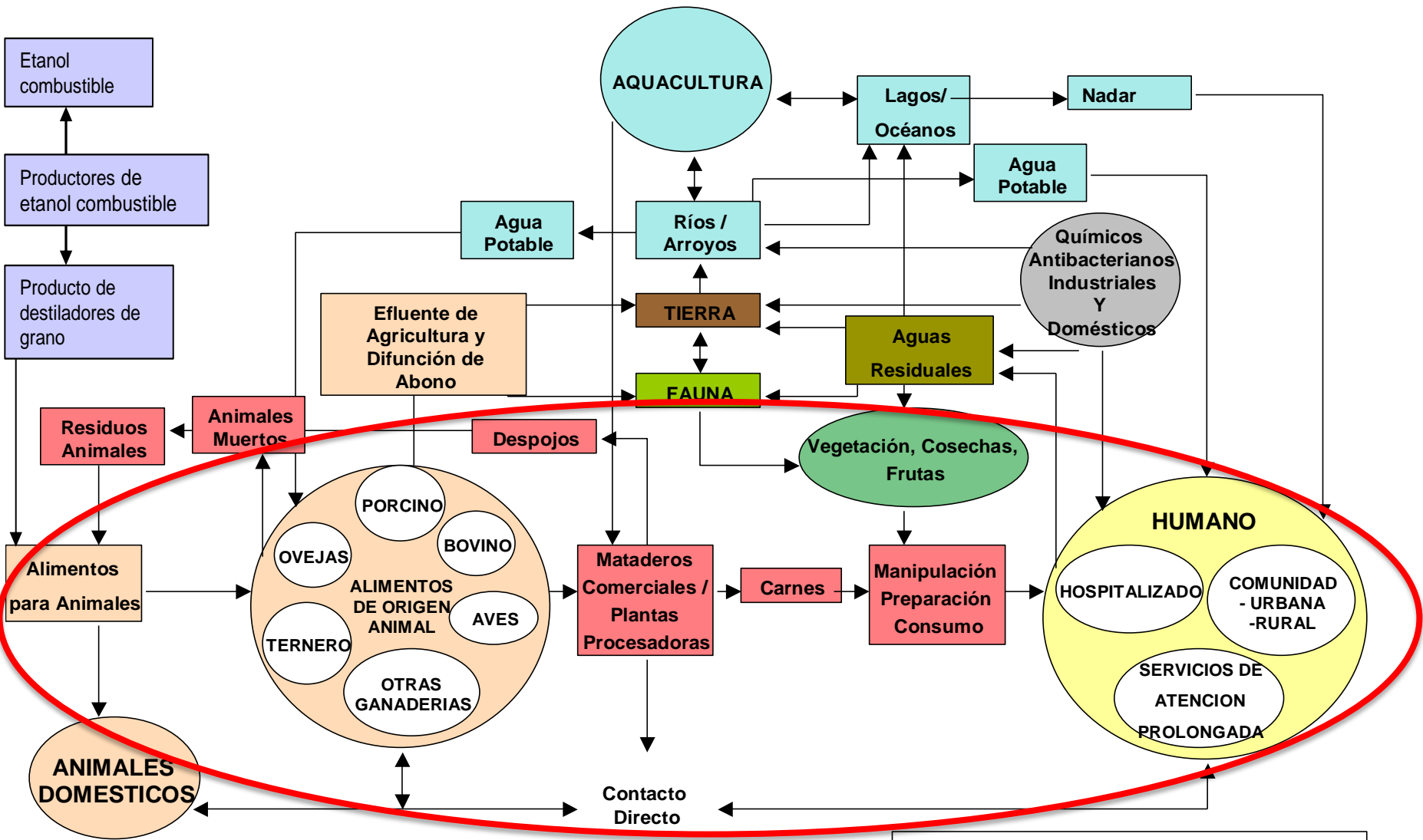


Epidemiología de resistencia antimicrobiana



Linton AH (1977), modificado por Irwin RJ

Epidemiología de resistencia antimicrobiana



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Canadian Food Animal Agriculture

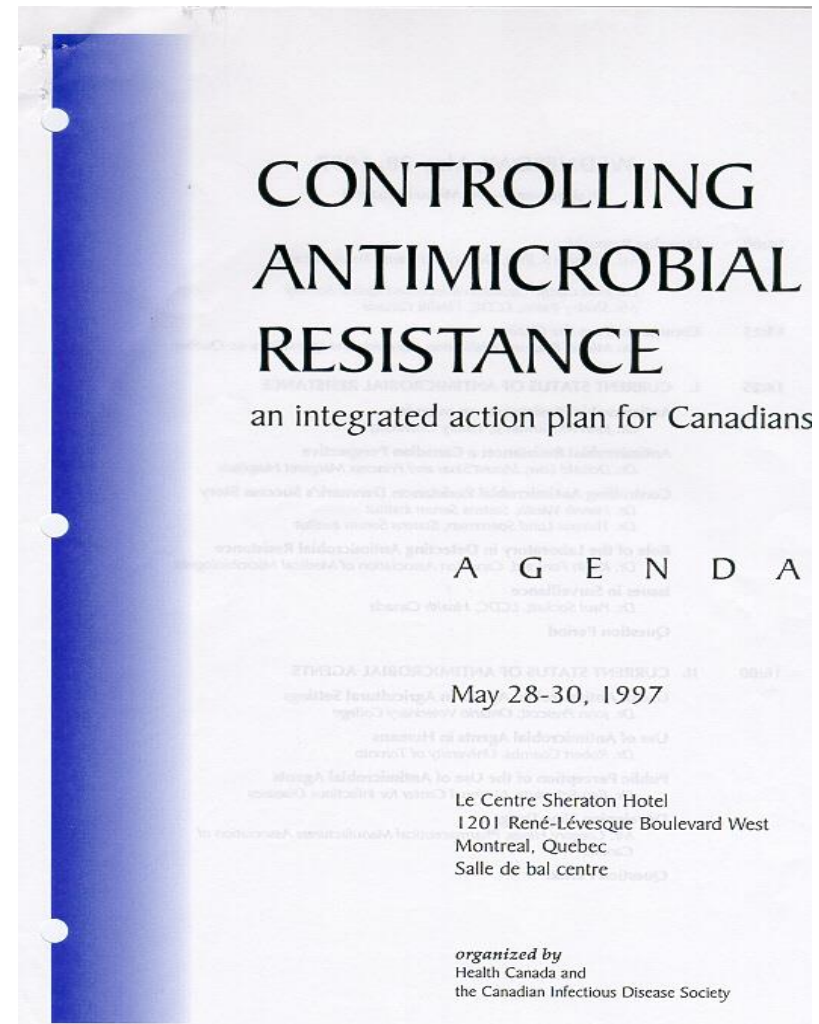
- Large geographical area
- Public Health Agency of Canada - national
- 10 provinces & 3 territories
 - Shared responsibility for health and agriculture
- Major livestock commodities
 - Beef cattle
 - 11 million
 - Pigs
 - 13 million
 - Chickens
 - 700 million broiler chickens



Conferencia de Consenso en Montreal, Mayo 1997

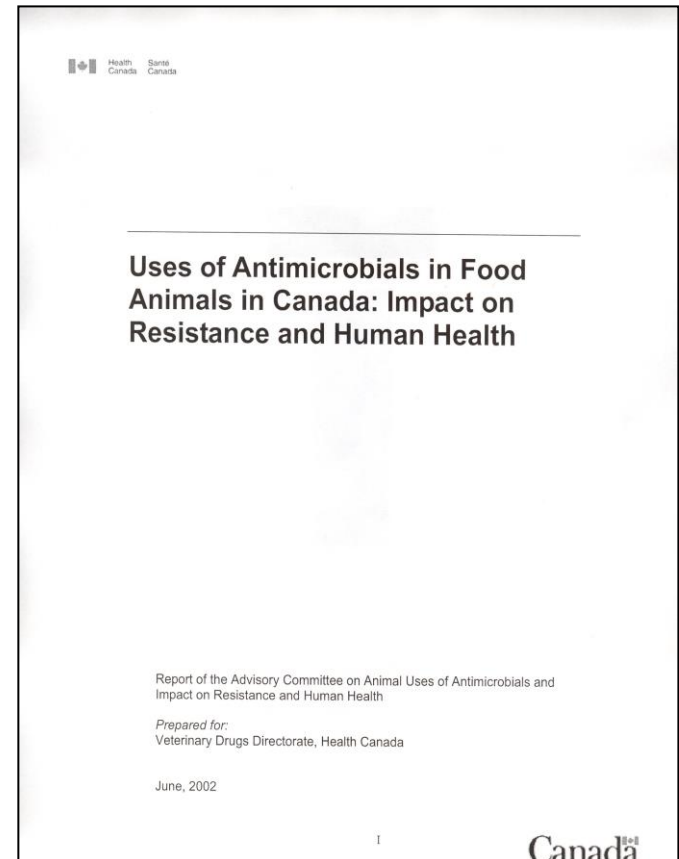
27 recomendaciones

“ Establecer un sistema de vigilancia al nivel nacional para monitorear resistencia a los antibióticos y su uso en los sectores agricultores y acuicultura ...”



Comité Consultivo en el Uso de Antibióticos en Animales y su Impacto en la Resistencia y Salud Humana, 2002

- Diseñar e implementar un programa nacional del monitoreo del uso de antibióticos en la producción animal
- Diseñar e implementar un sistema de vigilancia nacional continuo y permanente de la resistencia a los antibióticos que surga de la producción de alimentos de origen animal



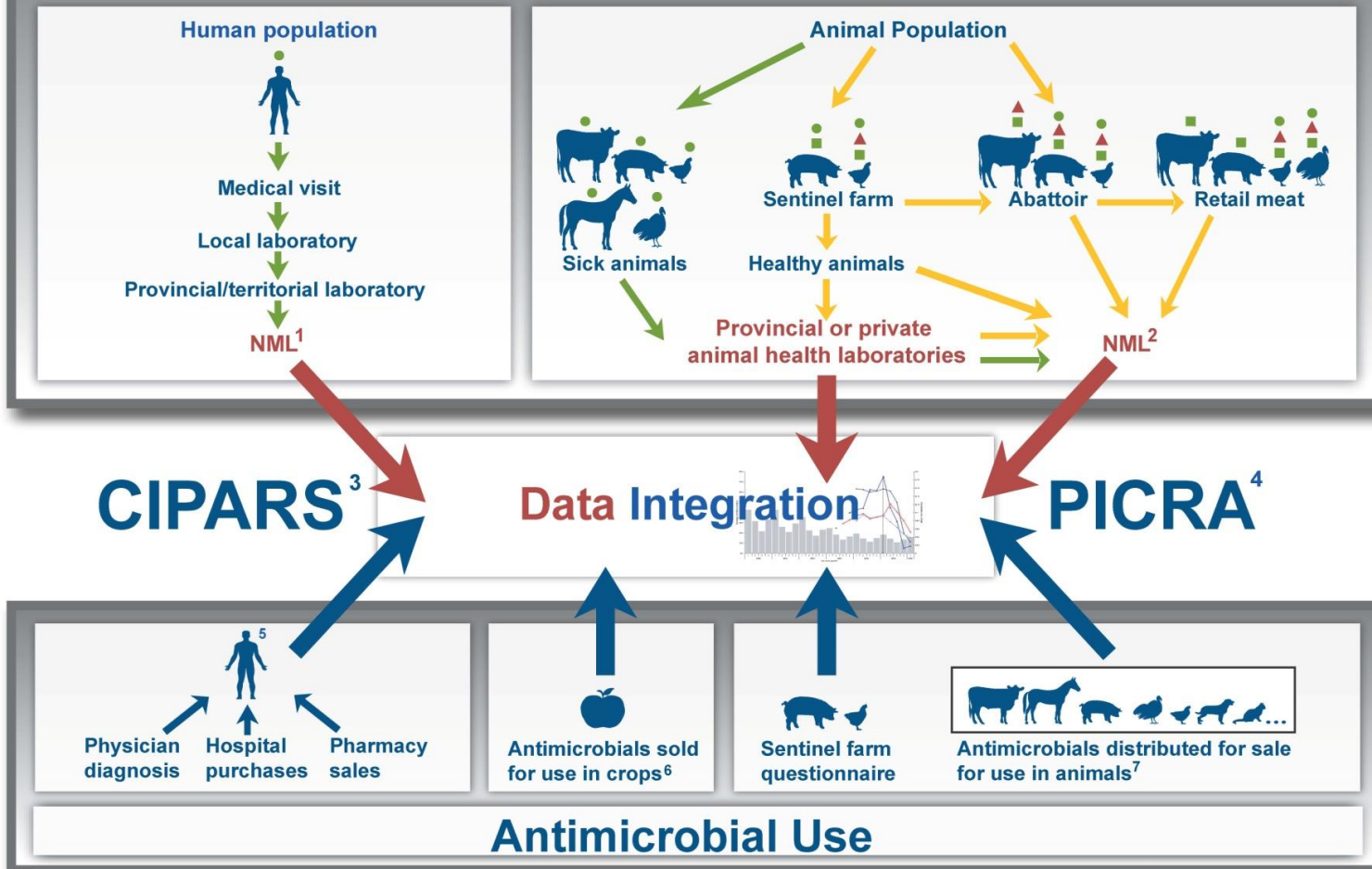
CIPARS Objectivos

- Proporcionar un enfoque unificado para observar las tendencias de AMR y de la utilización de antimicrobianos en los seres humanos y animales
- General información para facilitar la evaluación del impacto en la salud pública de los antimicrobianos utilizados en los sectores humanos y agrícolas
- Permitir con precisión comparaciones internacionales con otros países que utilizan sistemas de vigilancia similares (e.g., E.U.A. (NARMS), Dinamarca (DANMAP))

CIPARS

- Coordinado por PHAC
 - NML (LNM): Laboratorio Nacional de Microbiología
 - CFEZID: Centro de Enfermedades transmitidas por Alimentos, Ambiente y Zoonosis
 - Epidemiólogos, microbiólogos, biólogos
 - Veterinarios especializados
- Colaboradores:
 - Health Canada – Veterinary Drugs Directorate
 - Canadian Food Inspection Agency
 - Agriculture & AgriFood Canada
 - Ministerios de Agricultura y Salud Pública
 - Academia
 - Industria privada

Antimicrobial Resistance



1 National Microbiology Laboratory, Winnipeg, Manitoba, Public Health Agency of Canada (PHAC)
 2 National Microbiology Laboratory, Guelph (Ontario) and Saint-Hyacinthe (Québec)
 3 Canadian Integrated Program for Antimicrobial Resistance Surveillance, PHAC
 4 Programme intégré canadien de surveillance de la résistance aux antimicrobiens, Agence de la santé publique du Canada
 5 Canadian Antimicrobial Resistance Surveillance System (CARSS), PHAC
 6 Pest Management Regulatory Agency, Health Canada
 7 Canadian Animal Health Institute (CAHI)

- ➔ Active Surveillance
- ➔ Passive Surveillance
- *Salmonella*
- ▲ *Campylobacter*
- *Escherichia coli*

Investigation and design phase

Human AMU data

CAHI AMU data

Crop AMU data

1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017

National
Consensus
Conference

WHO Global Strategy for
the Containment of
Antimicrobial Resistance

HC AMR Advisory Committee
on Animal Uses of
Antimicrobials and Impact on
Antimicrobial Resistance and
Human Health

Farm – Turkey AMU/AMR

Farm – Broiler chicken
National AMU/AMR

Retail – added Turkey

Retail – added Fish/Shrimp

Retail – added Maritimes

Retail – added BC

Farm - Pigs National AMU/AMR

Retail – added Saskatchewan

Retail – Beef, Chicken, Pork Ontario & Québec
Human Clinical (Enhanced Passive) National
Human AM Use National

Abattoir - Beef Cattle, Chickens, Pigs National
Animal Clinical (Passive) National

CIPARS Evolution

Investigation and design phase

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Crop AMU data

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National AMU/AMR

Retail – added Turkey

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Retail – suspended Maritimes in 2015

Retail – added BC

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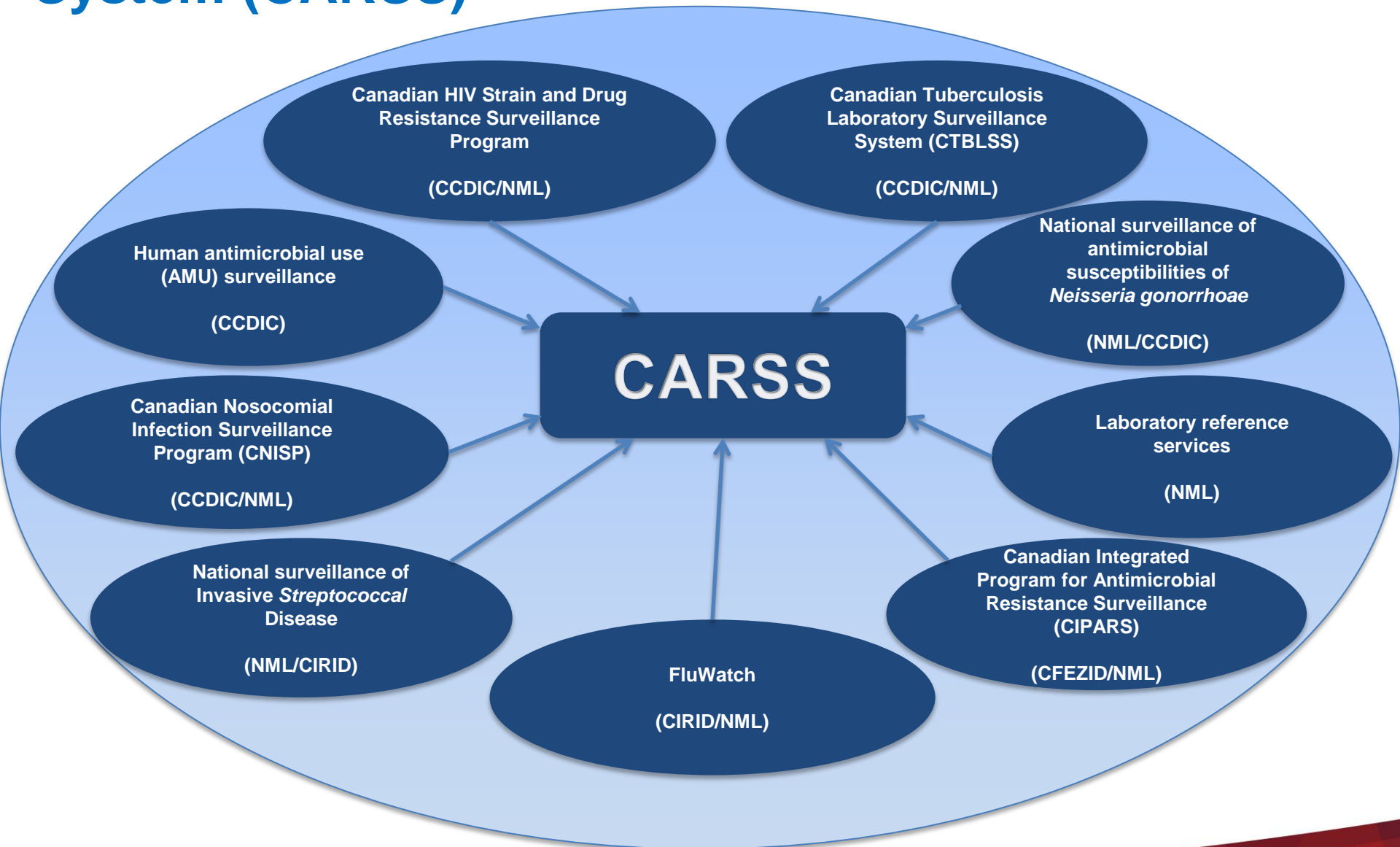
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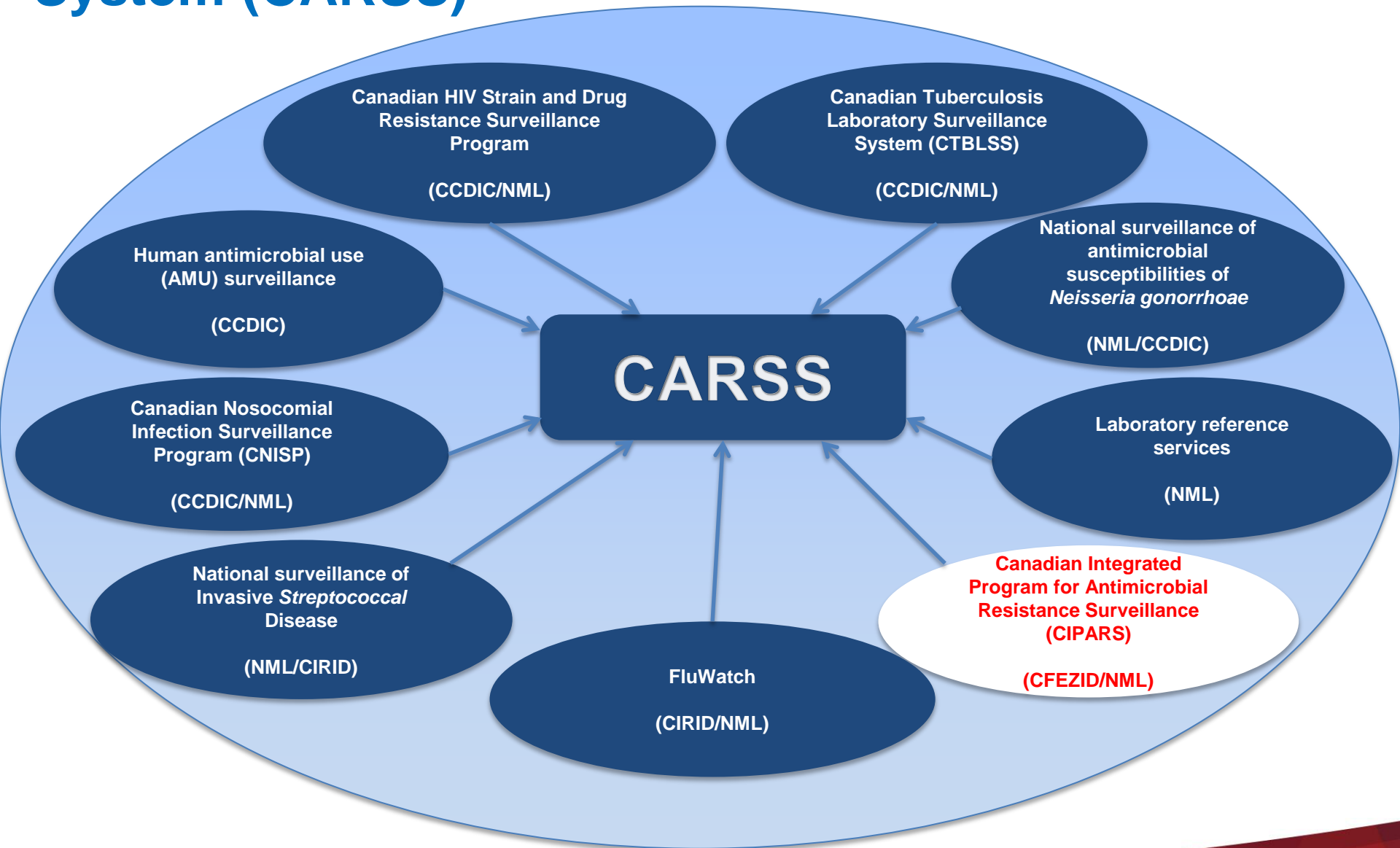
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CIPARS Evolution

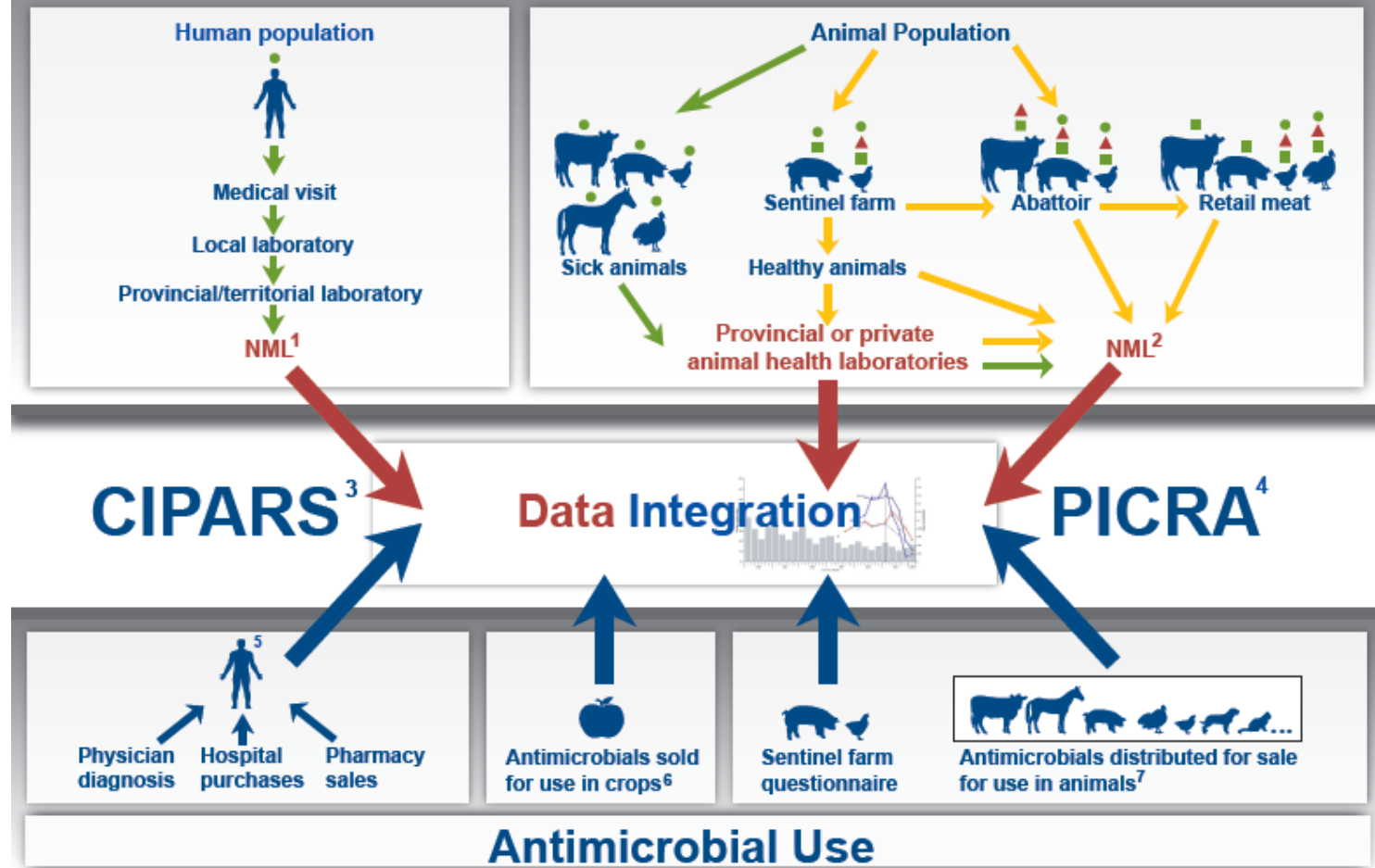
Canadian Antimicrobial Resistance Surveillance System (CARSS)



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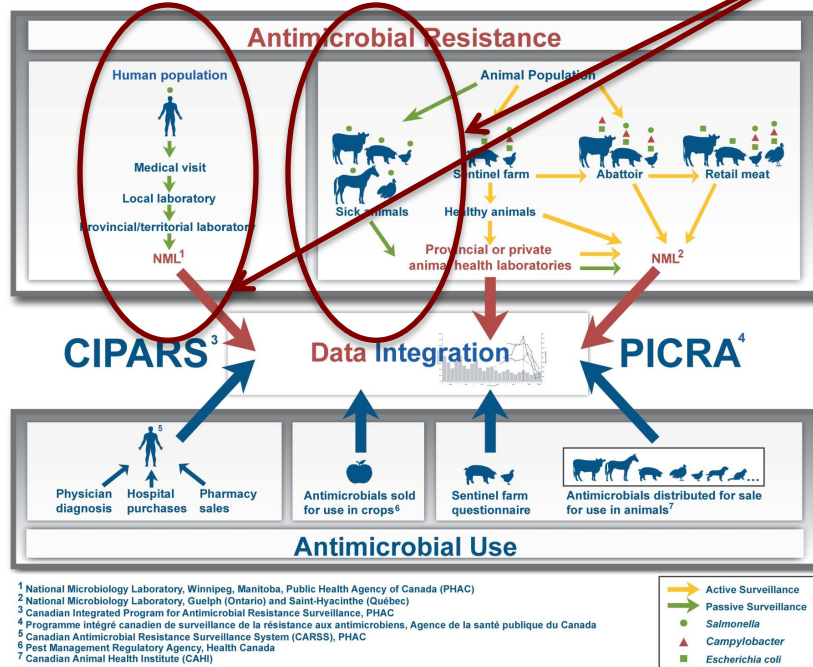
Antimicrobial Resistance



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CIPARS



Datos diagnosticos clinicos - vigilancia en los sectores humano y animal

- Laboratorios de salud humana al nivel de provincia mandan cepas de *Salmonella* al LNM
- Laboratorios de salud animal privados ó al nivel de provincia mandan cepas de *Salmonella* al LNM

Vigilancia en el sector humano

- Colección de datos empezó el 1^{ero} de enero 2003
- Información epidemiológica que acompaña a las cepas
- **Mandatoria:** Fecha recibida, edad, sexo, provincia/territorio, ciudad, serotipo
- **Opcional:** Fecha de inicio de enfermedad, hospitalización, viajes, tratamiento con antibióticos, brote
- BC, AB, ON, QC: Todas las cepas (brotes y esporádicos) que recibieron del primero al quince de cada mes, y todos los *S. Newport* y *S. Typhi* recibidos durante el período de vigilancia entero; SK, MB, NB, NL, NS, PE: Todas las cepas de *Salmonella* (brotes y esporádicos) recibidos durante el período de vigilancia entero
- Desde el 2010
 - Heidelberg, Enteritidis, Newport, Typhimurium, 4,[5],12:i:-, Typhi, Paratyphi A and B

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FoodNet Canada



Calgary AB

Fraser Valley BC

London ON

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As of mid 2017 all human *Salmonella* isolates are being whole genome sequenced by PulseNet Canada

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But.....Culture Independent Testing is beginning to have an effect

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But.....Culture Independent Testing is beginning to have an effect

Human *Campylobacter* from three FoodNet Canada sites

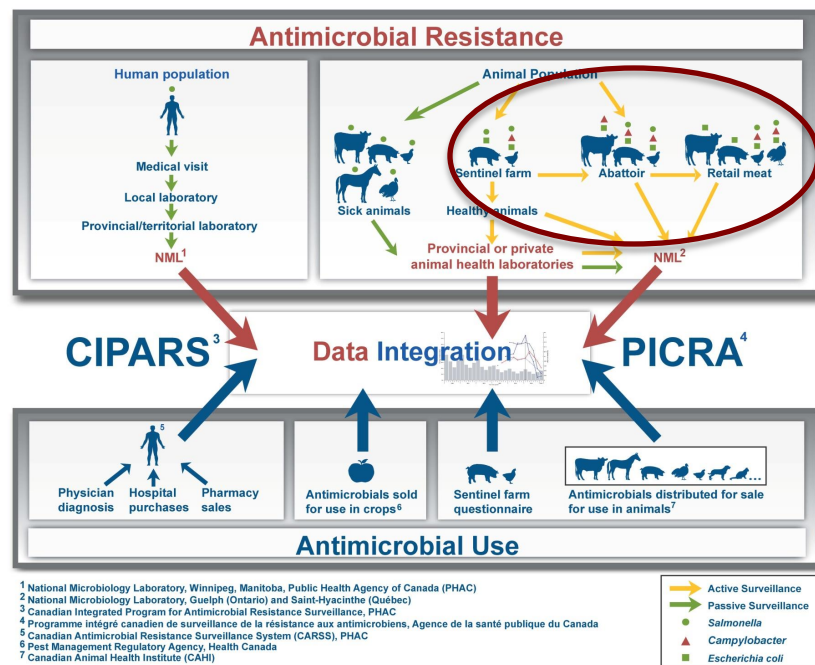
Datos diagnósticos clínicos - vigilancia en el sector animal

Objetivo

- Patrones de resistencia nuevos ó emergentes
- Nuevas combinaciones de serotipos y patrones de resistencia dentro de las cepas de *Salmonella*
- Las muestras diagnósticas veterinarias las colectan los veterinarios y/o los productores Las muestras de diagnóstico animal son recolectadas por veterinarios y/o productores
- Laboratorios de salud animal privados ó al nivel de provincia
- BC, ON y QC tratan de mandar todas las cepas

CIPARS

AMR Surveillance – Food Chain

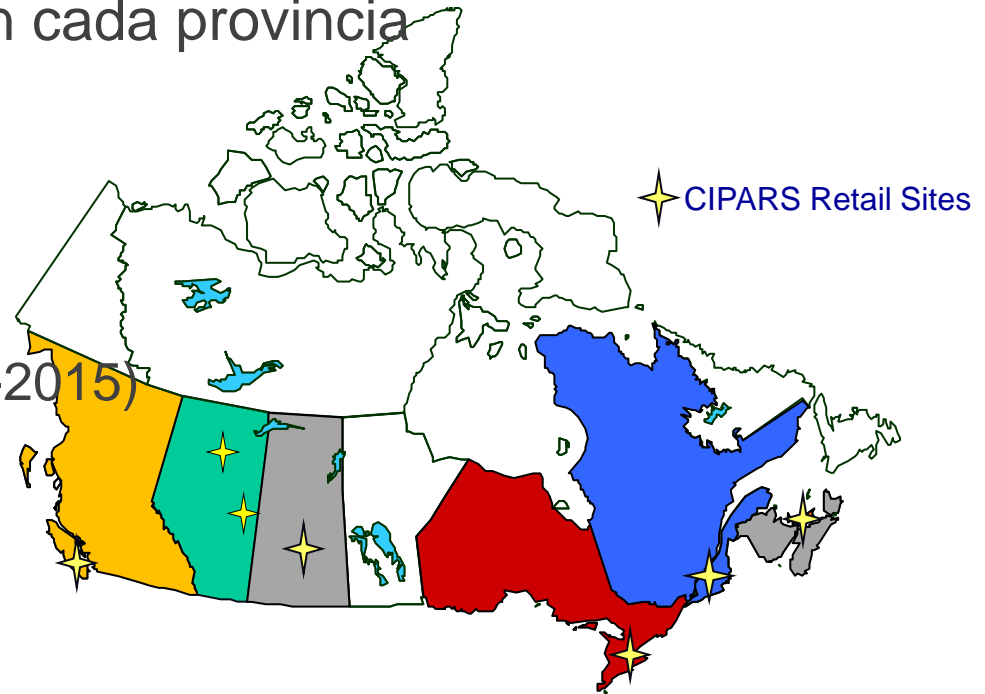


- Organisms: *Salmonella*, *Campylobacter*, and generic *E. coli*; others

- Fecal samples are collected on farms (voluntary)
- Cecal content samples are collected from federally inspected abattoirs (voluntary)
- Fresh meat samples are purchased at the grocery store
- Raw fruit, vegetables, herbs & spices (CFIA) (survey)
- Animal feed (CFIA) (monitoring)

CIPARS Vigilancia venta al detalle

- Selección aleatoria de división de censo y asignación de muestreo dentro de las divisiones basado en la población del censo
- 15-20 divisiones de censo en cada provincia
- Provincias
 - Ontario, Québec (2003)
 - Saskatchewan (2005-2015)
 - British Columbia (2008)
 - Provincias Marítimas (2009-2015)
 - Alberta (2014)
- Muestreo continuo
 - Semanal en ON, QC, AB
 - Cada otra semana en BC, SK y las provincias Marítimas
 - Objetivo: 100 cepas/comodidad/provincia/año



CIPARS Vigilancia venta al detalle

Bacteria de interes por comodidad

	<i>Salmonella</i>	<i>E. coli</i> (genérico)	<i>Campylobacter</i>
Pollo [piernas & alas]	★	★	★
Pavo [molida]*	★	★	★
Cerdo [chuleta de hombro]	★	★	-
Carne [molida**]	-	★	-

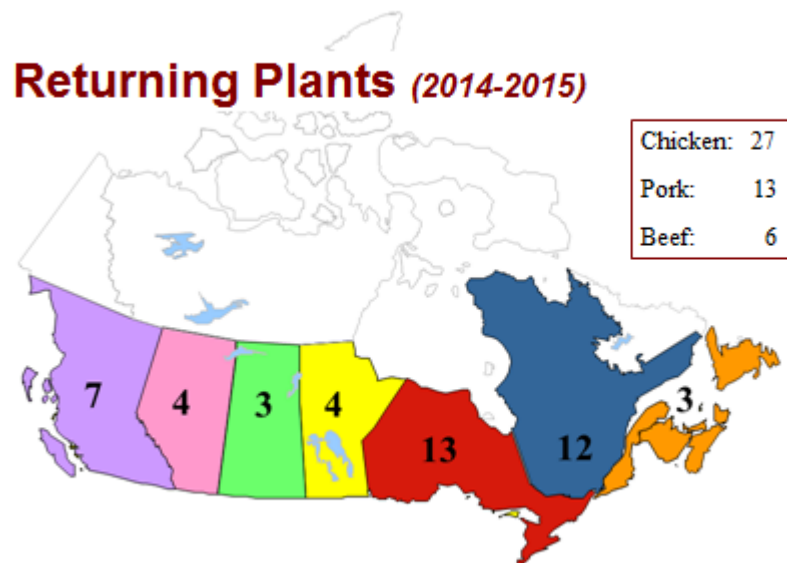
* 2011

** Selección sistemático de tipos de carne molida

A partir del 1^{ero} de enero 2010 no se hacen pruebas para detectar *Enterococcus* spp.

CIPARS Vigilancia en mataderos

- Mataderos que se inspeccionan al nivel federal
- Mataderos seleccionados aleatoriamente basados en el volumen de animales
- Muestreo anual proporcional a los volúmenes de animales que se procesan
- Períodos de muestreo para cada matadero se distribuye dentro de 12 meses
- Muestras digestivas
 - el intestino ciego
- Ganado, pollos y cerdos
- Tamaño de muestra calculado para obtener:
 - 150 cepas de *Salmonella* e *E. coli*; 100 cepas de *Campylobacter*
- Provincia de origen = último lugar de residencia del animal



CIPARS Vigilancia en mataderos

Bacteria de interes por comodidad

	<i>Salmonella</i>	<i>E. coli</i> (genérico)	<i>Campylobacter</i>
Pollos [de engorde]	★	★	★
Cerdos [de mercado]	★	★	★
Ganado [carne y leche]		★	★

Aislamiento de *Salmonella* en carne no se lleva a cabo debido a la baja prevalencia

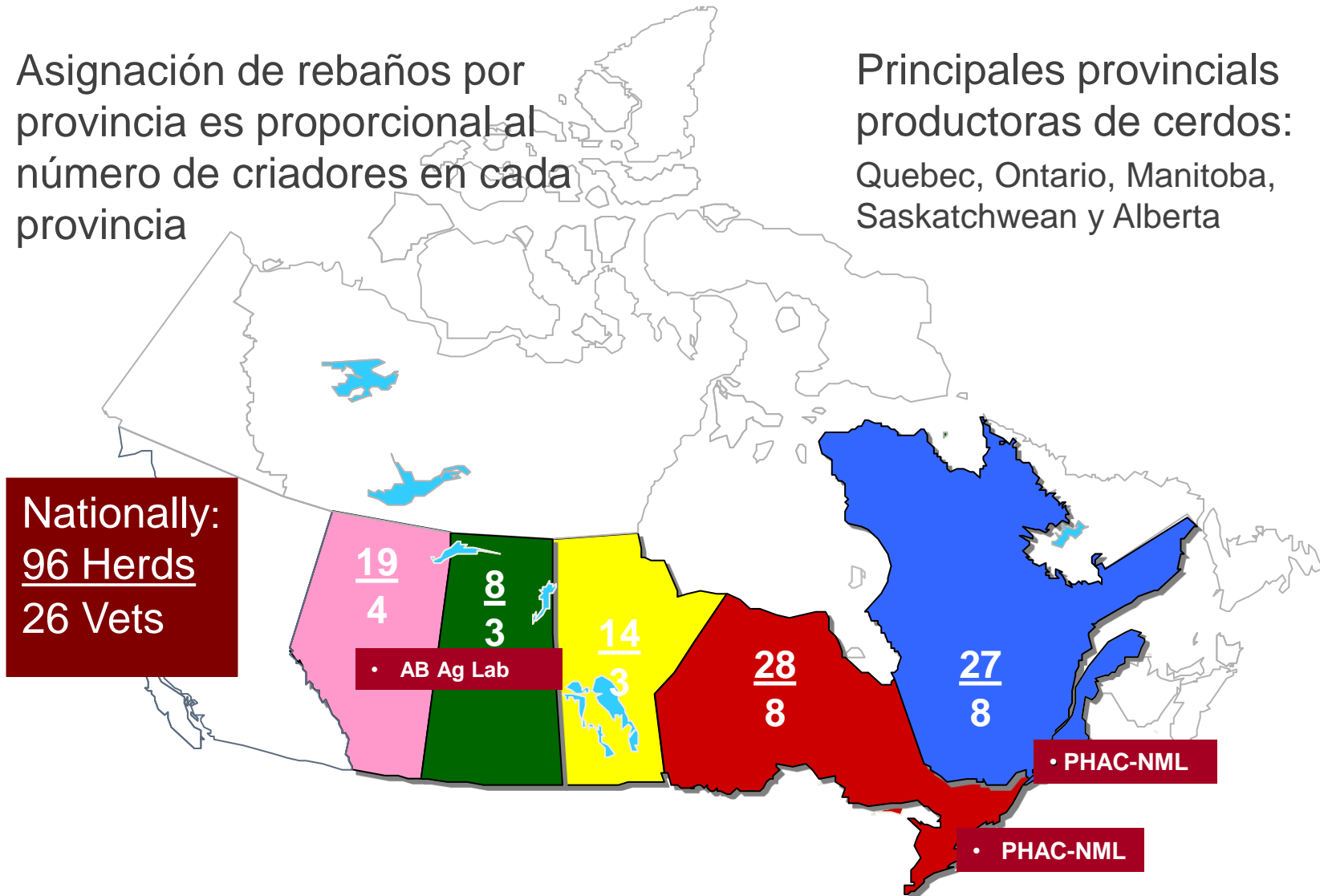
CIPARS Vigilancia en granjas

- Veterinarians collect samples & data
- Specified inclusion and exclusion criteria for herd/flock enrollment
- Veterinarians and producers paid for voluntary participation
- Developed using extensive consultation with producers, veterinarians, and commodity groups in order to have a sustainable and practical program
- Commodities
 - Grower-finisher swine - National (2006)
 - Broiler chickens - National (2013)
 - Turkey – FoodNet Canada Sentinel Sites (2014)
 - Feedlot Beef – FoodNet Canada Sentinel Site (2016)
 - Dairy under development

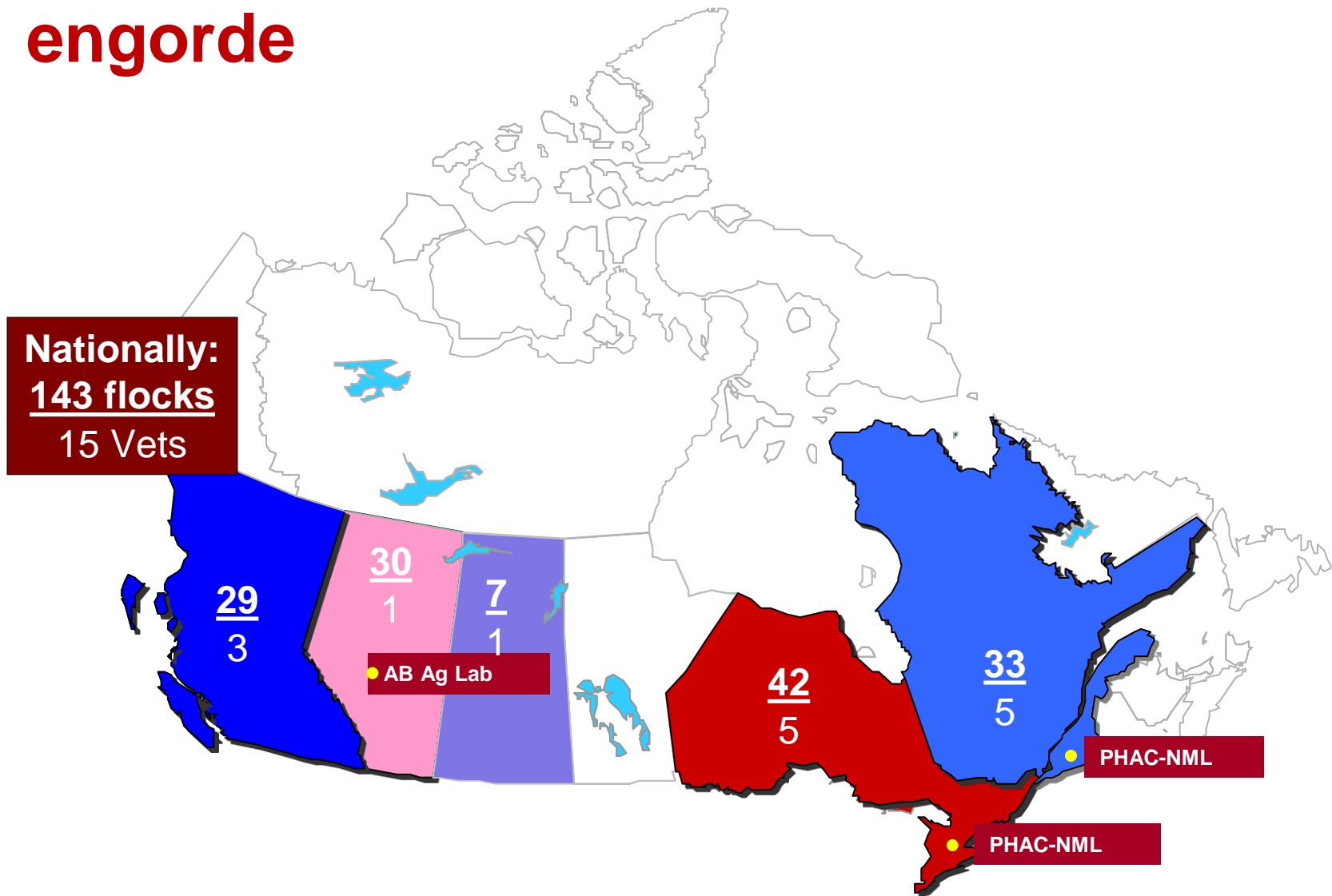
CIPARS Vigilancia en granjas de cerdos

Asignación de rebaños por provincia es proporcional al número de criadores en cada provincia

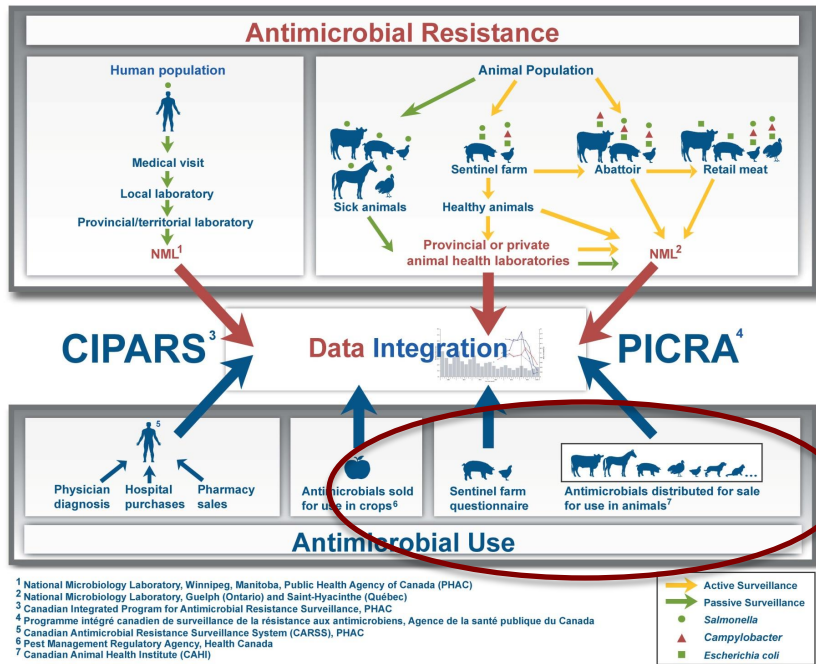
Principales provinciales productoras de cerdos: Quebec, Ontario, Manitoba, Saskatchewan y Alberta



CIPARS Vigilancia en granjas de pollos de engorde



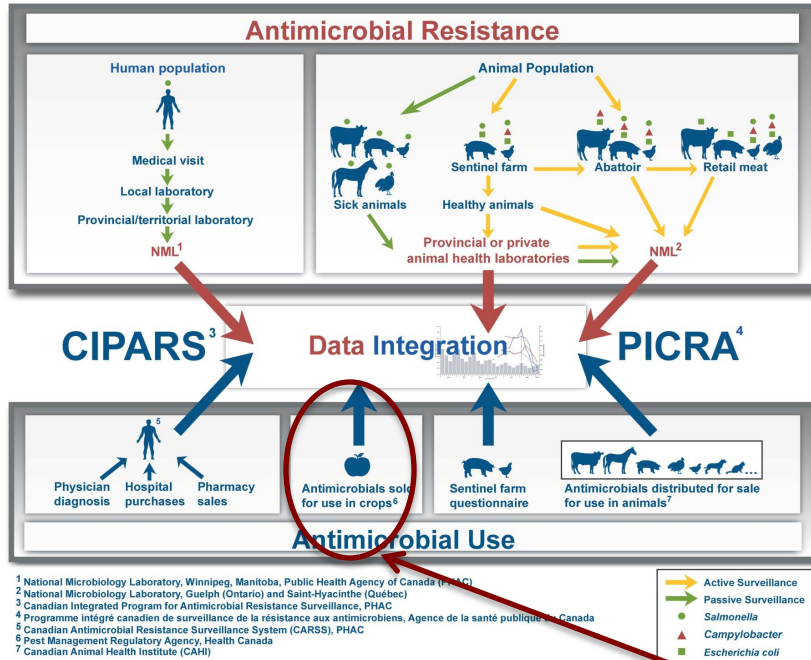
CIPARS



Uso de antimicrobianos en animales

- Antimicrobials used, reason for use and farm information collected from CIPARS farms
- Antimicrobials distributed for sale in animals - data provided by the Canadian Animal Health Institute, by species, aggregated to drug class
- Companion animal Rx - pharmacies – IMS Health (Canada)

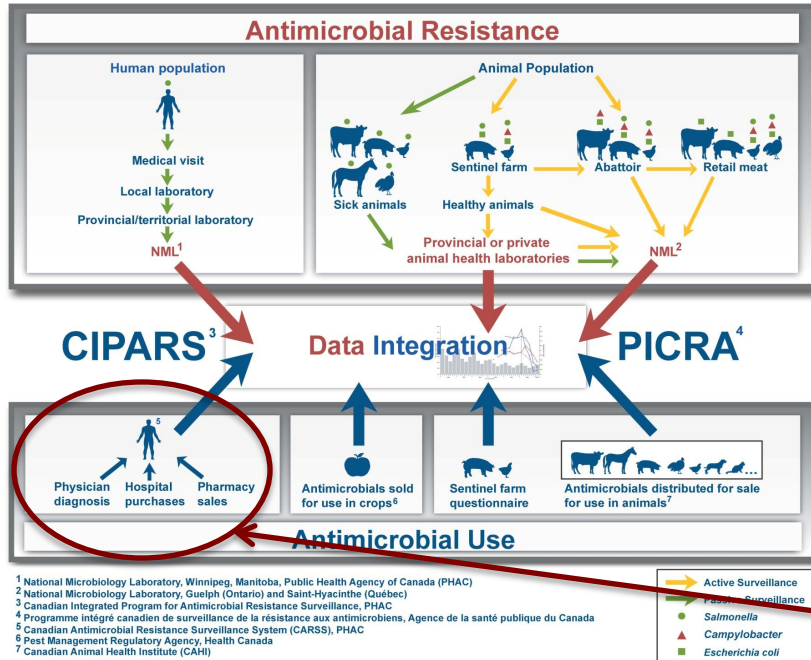
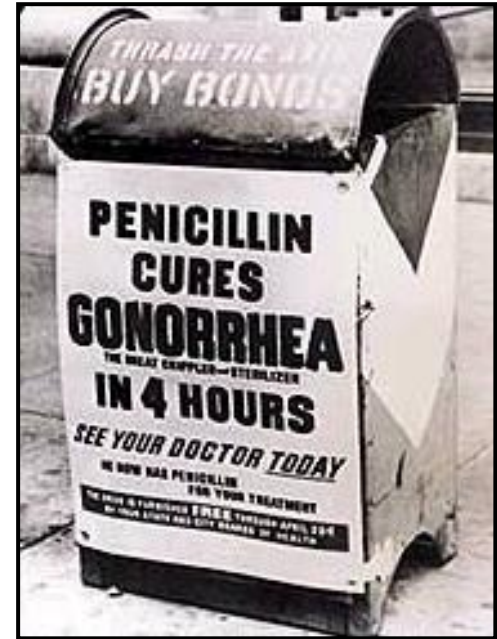
CIPARS



Antimicrobial Use - Crops

- Aggregated data on Antimicrobials sold for use as pesticides on crops (apples, pears, tomatoes, peppers, eggplants, and walnuts) provided by PMRA

CIPARS



Uso de antimicrobianos – sector humano

- IMS Health (Canada) → Canadian Antimicrobial Resistance Surveillance System - CARSS

Vigilancia de uso de antimicrobianos – sector humano

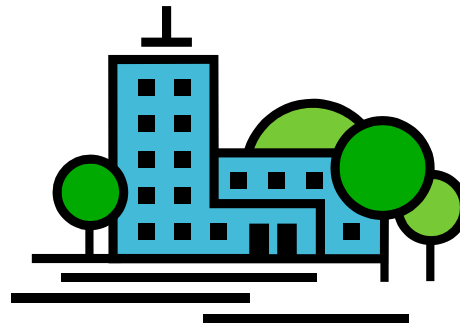


Farmacias

Dispensación en farmacias (CSC)

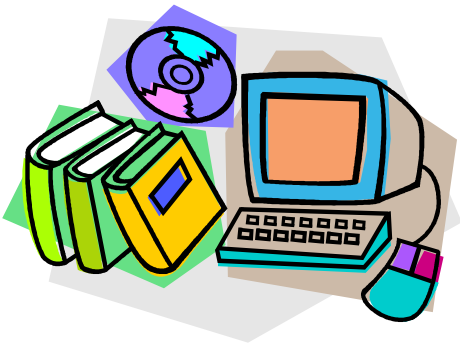
Compras de farmacia y hospitales (CDH)

Diagnóstico y recetas – Clínicas (CDTI)



IMS Salud Canadá

Reune y acumula datos



PHAC

Clasificación, análisis e interpretación

Reportes anuales

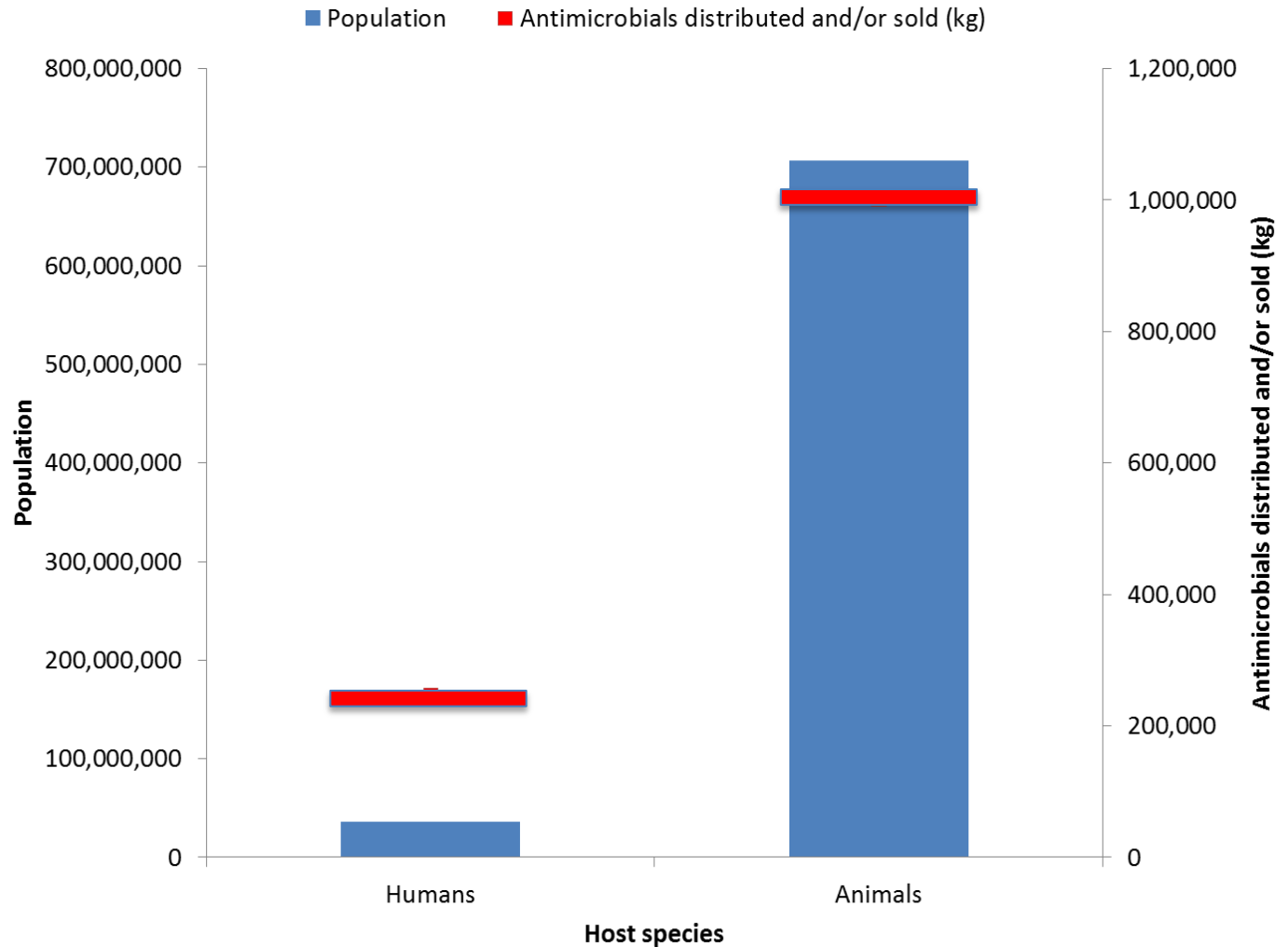
Colaboraciones

Publicaciones

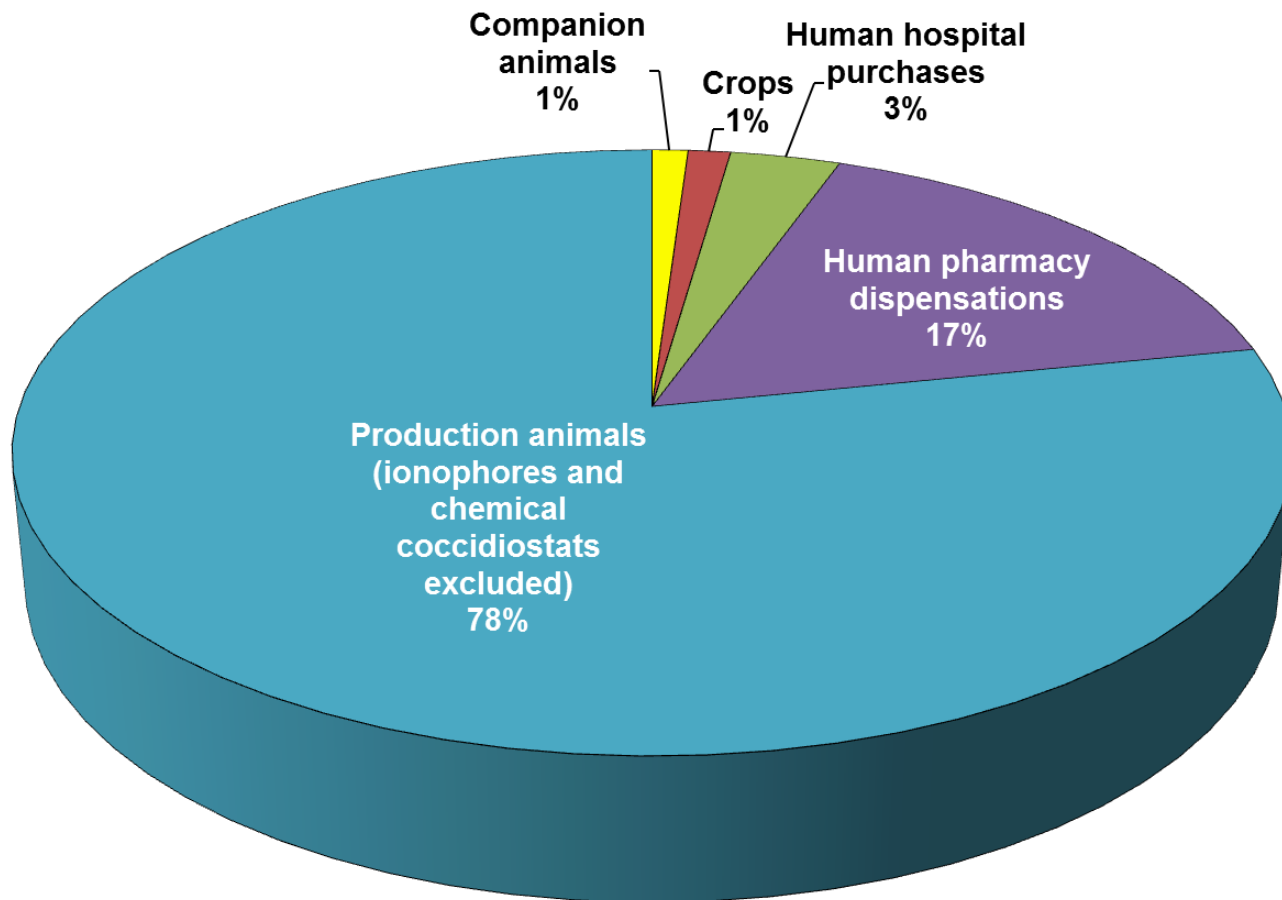
Population size and antimicrobial quantities

~ 1.5 times more antimicrobials were distributed for use in animals than humans on a per kg host basis (European standard weights of animals)

Animal distribution data does not include own use or active pharmaceutical ingredient importation



Antimicrobials distributed / sold in Canada (kg active ingredient)



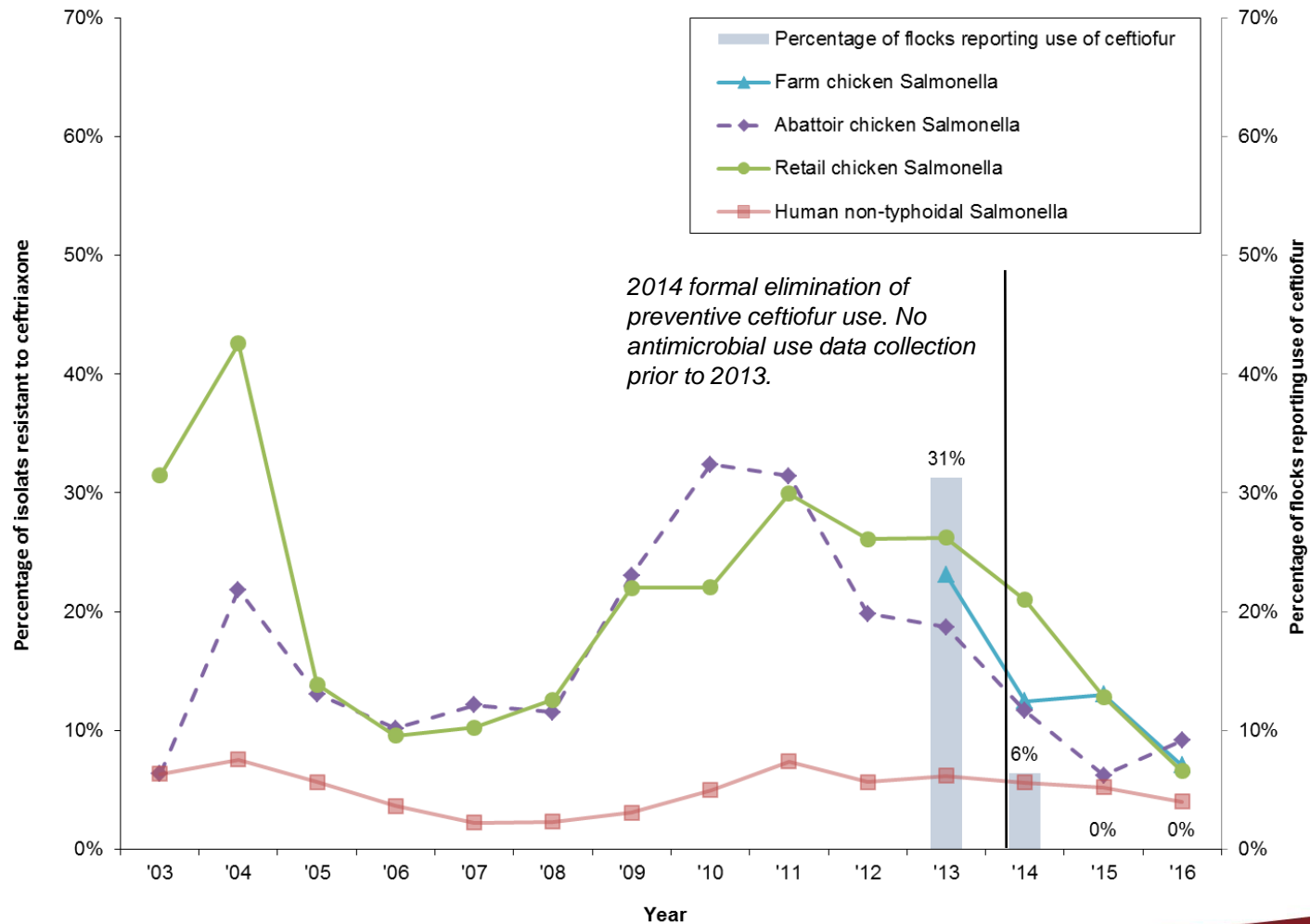
Animal distribution data does not account for quantities imported for own use or as active pharmaceutical ingredients for further compounding.

Ceftriaxone resistance in *Salmonella* & *E. coli*

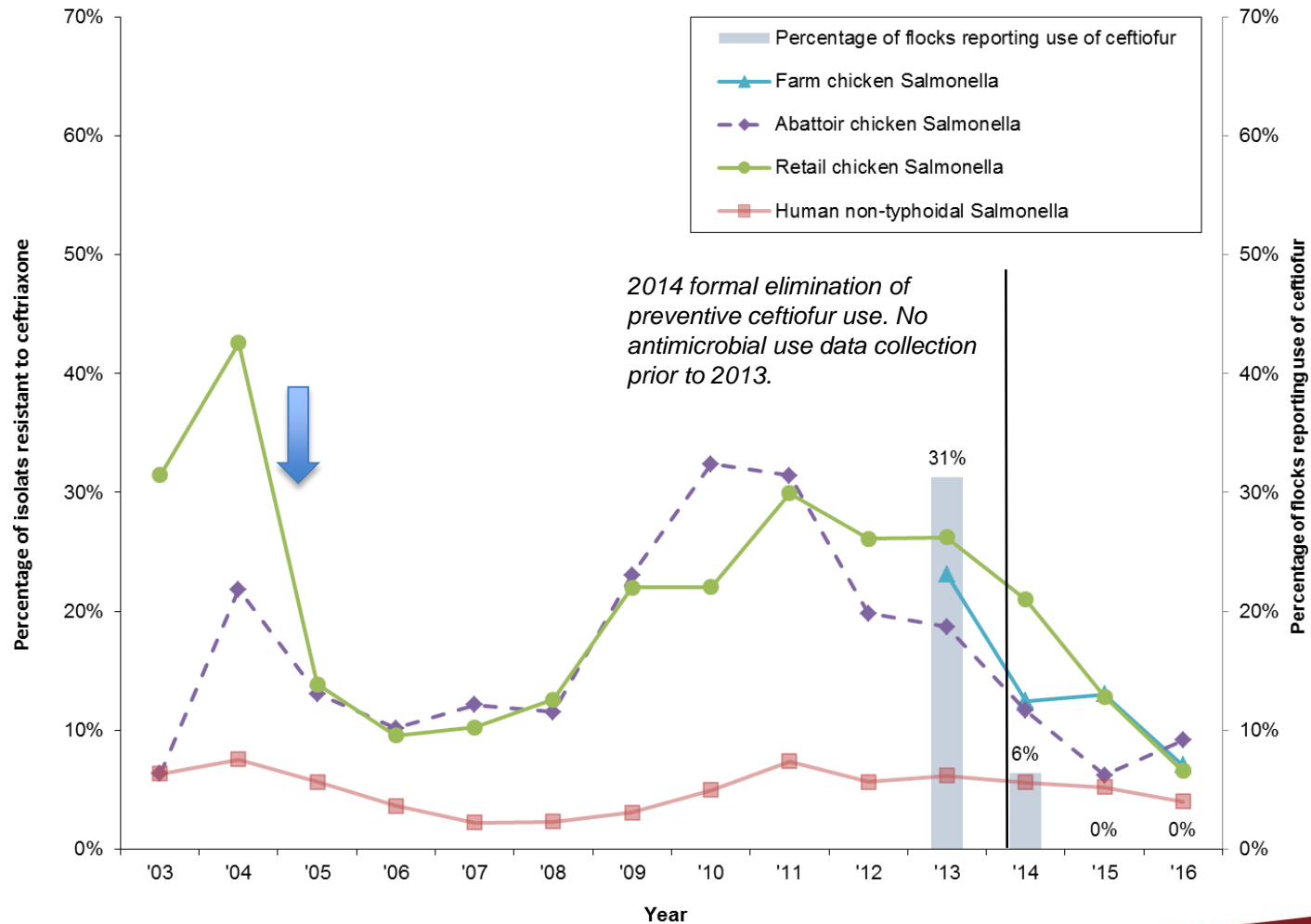
Ceftriaxone/Ceftiofur - 3rd generation cephalosporins

- » Ceftriaxone used to treat a variety of human infections
- » Ceftiofur used to treat a variety of animal infections
- » Ceftiofur preventive use *in ovo* or in hatched broiler chicks in Canada was extra-label

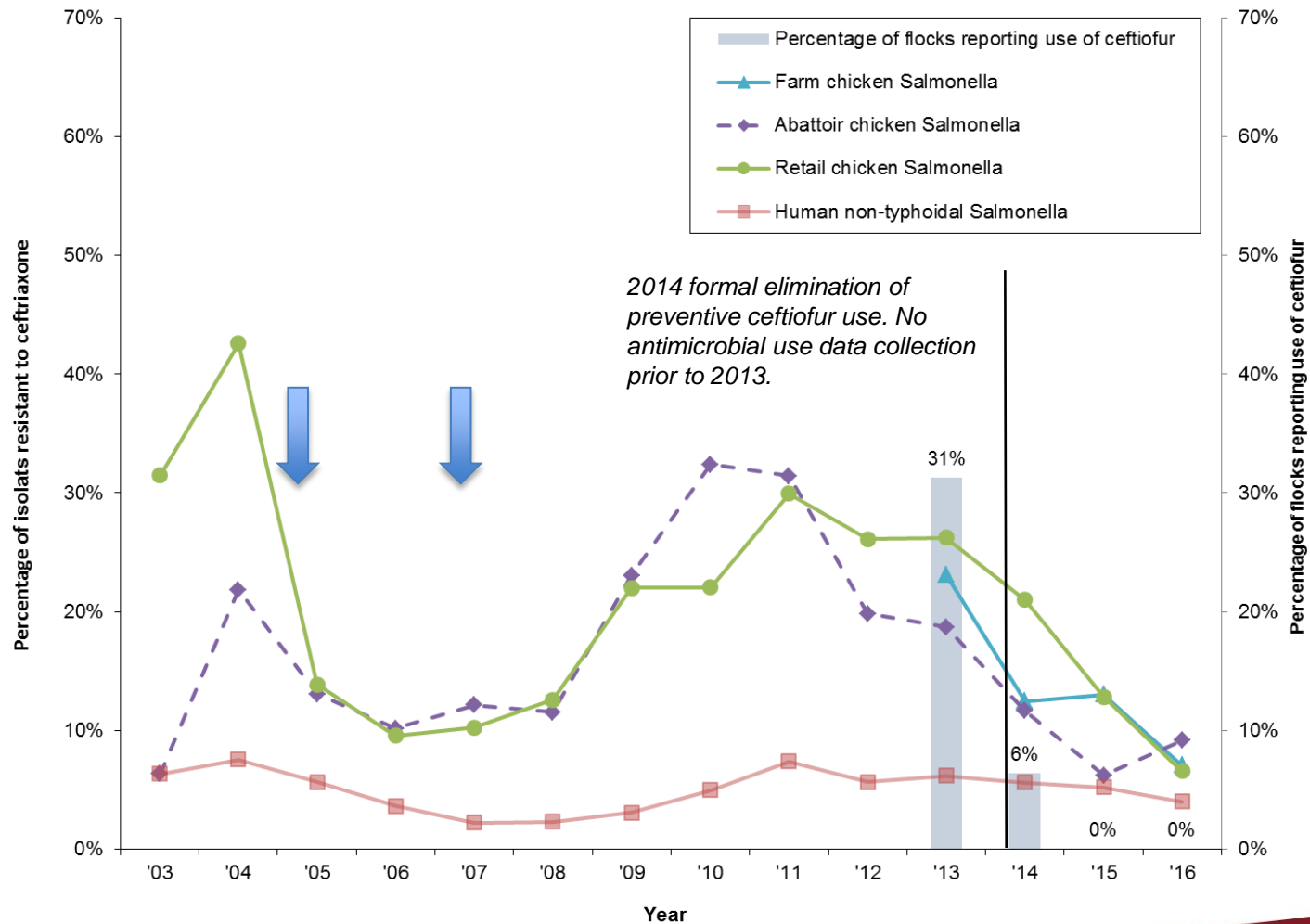
Reduction in reported use of ceftiofur on farm and changing resistance to ceftriaxone in *Salmonella* from humans and chicken



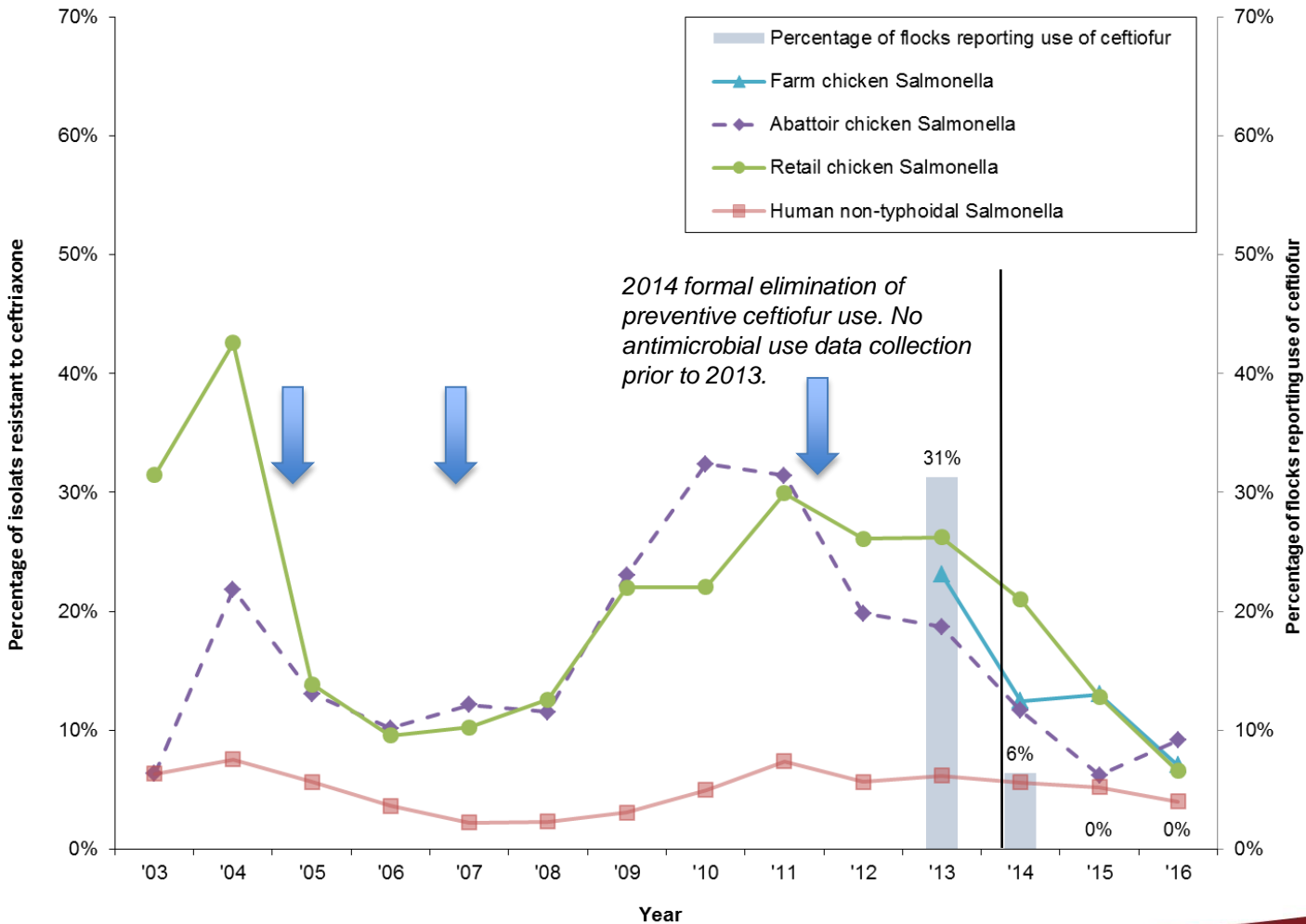
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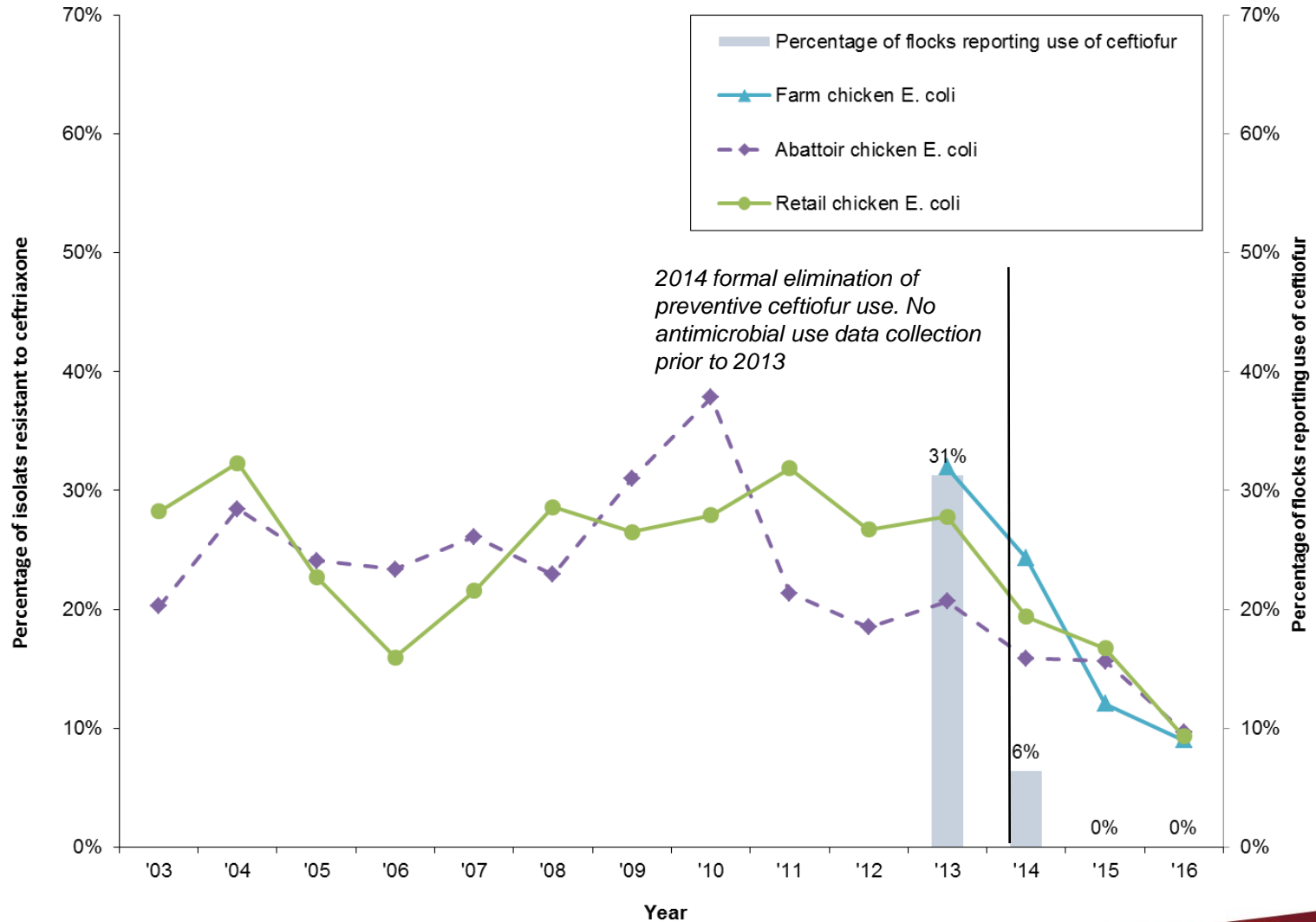
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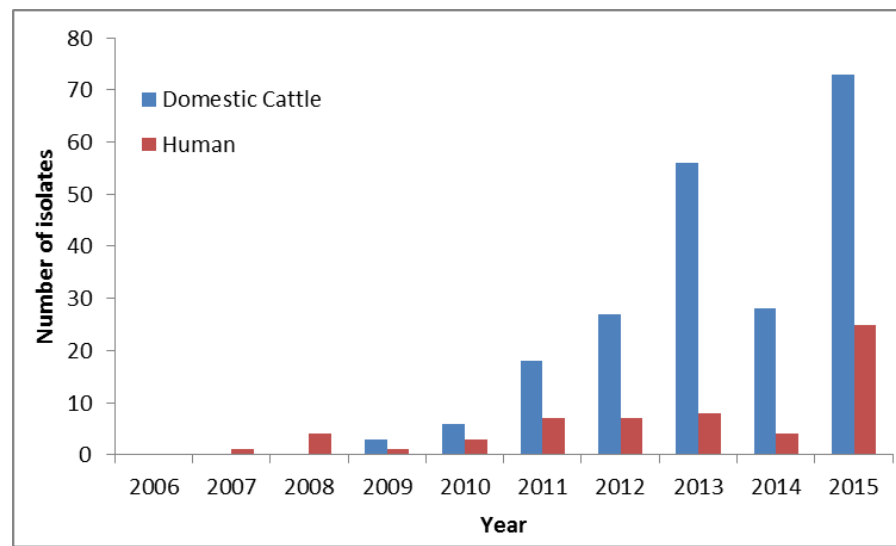
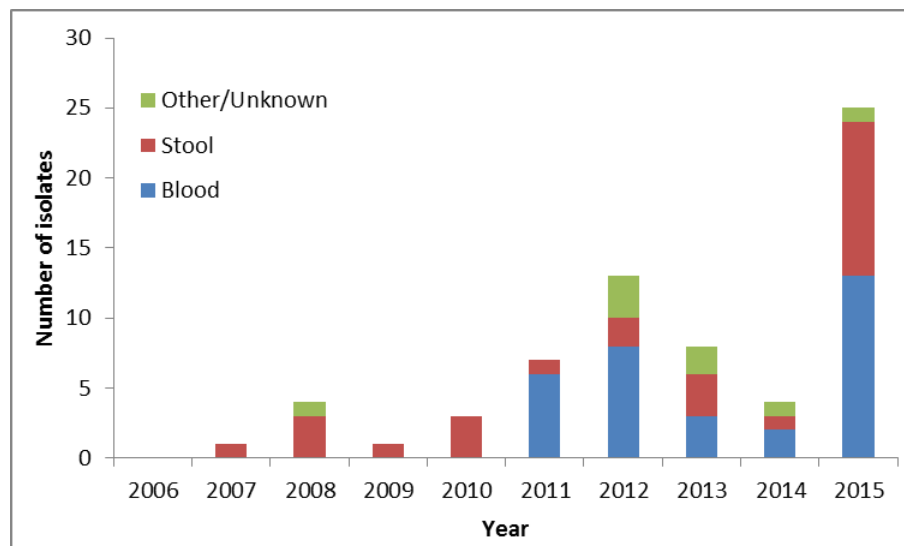


Declining resistance to ceftriaxone in *E. coli* from chicken and reported decrease in use of ceftiofur



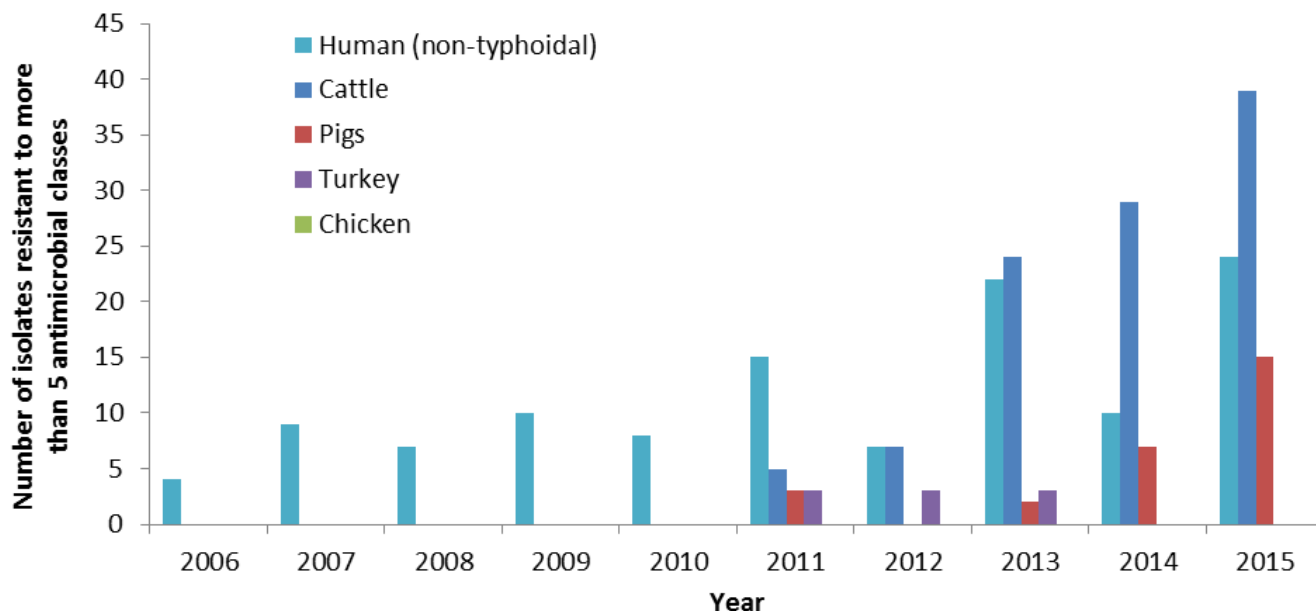
Clinical *Salmonella* Dublin in humans and cattle

Increase in *Salmonella* Dublin human infection numbers – high proportion are blood stream



- Since 2006, 28% (59/211) of cattle isolates and 22% (13/60) of human isolates resistant to more than 5 antimicrobial classes
- 2015, 30% (22/73) of cattle isolates and 28% (7/25) of human isolates were resistant to more than 5 classes

Highly resistant agri-food *Salmonella* isolates



- resistant to > 5 antimicrobial classes
- Most of the highly resistant agri-food isolates have been recovered from clinically sick cattle (n=104)
 - 57% were Typhimurium and 37% were Dublin
- No highly resistant *Salmonella* isolates from chicken sources

Carbapenemase-producing enterobacteriaceae (CPE) from the food chain

- Screening of isolates from human (2010) and agri-food sources from CIPARS (2012) core surveillance using MIC criteria and disk diffusion testing followed by molecular based gene characterization
- Additional retail samples were collected for targeted carbapenem resistance screening using selective media:
 - Dried chicken jerky pet treats (2013-2014)
 - Niche market fresh/frozen seafood (2015)
 - Imported dried spices (2015)
 - A subset of core retail samples (beef, chicken, pork, turkey 2014 + chicken 2012)
- Over 5000 isolates screened; 9 isolates had carbapenemase genes:
- All from imported seafood products (all selective media):
 - 1 NDM-1 from a mollusc – niche market sampling
 - 8 other carbapenem resistant organisms: 4 shrimp, 4 bi-valve molluscs
- None identified in *E. coli* or *Salmonella* from animals or food; none in *Salmonella* from humans



mcr-1

- CANWARD; 2008-16; 10-15 hospital sites (>6,000 isolates)
Walkty et al. CMAJ. 2016. 4:641-645.
- CNISP Carbapenemase Surveillance; 2007-16 (>500 isolates)
- CIPARS in 2016 and screened all human (n=4200) and agri-food *Salmonella* (n=3271) and *E. coli* (n=4507)
- Reference Services
- PulseNet WGS Analysis of existing *E. coli and Salmonella* (>5000)
- Toronto area sewage/recreational beach

mcr-1

• Human cases (5)

- *E. coli* - Toronto ON (2010); blood isolate from ER; **CANWARD**
- *E. coli* - Vancouver BC (2010); blood isolate from ER; **CANWARD**
- *E. coli* - Ottawa ON (2011); OXA-48 positive, pan-resistant; lived in Egypt for previous 5 years; **Reference Services**
- *Salmonella* Typhimurium - ON (2012); **CIPARS**
- *E. coli* - BC (2016); obtained health care in China; **Reference Services**

• Food/Animal (8 isolates)

- 2 *E. coli* - ON (2010); retail ground beef; 2 locations; **CIPARS**
- *E. coli* - ON (2012); retail veal; **CIPARS**
- *E. coli* - Vancouver BC (2015); retail soft shell turtle; **U of Sask study**
- *Salmonella* I:4,[5],12i:- - ON (2016); veal calf - clinical; **CIPARS**
- *E. coli* ON - (2016); retail abalone; **CIPARS**
- 2 *E. coli* - QC (2016); veal calf - abattoir; **U of Montreal/CIPARS**

• Environment (1 isolate)

- *E. coli* - Toronto ON (2012); sewage; **WGS GRDI study**

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- **Rita Finley – material in Spanish**
- **CIPARS – CFEZID, NML**
- **CIPARS Collaborators:**
 - » Human (AMR): Provincial Public Health Laboratories
 - » Farm (AMR and AMU):
 - The veterinarians, producers and commodity groups; Alberta Ag. And Sask Ag.
 - » Abattoir & Feed: CFIA, abattoir operators, samplers and personnel
 - » Retail: Participating health units, UPEI, UofGuelph, CCH
 - » Clinical Animal Isolates: Provincial Animal Health Laboratories
 - » Antimicrobial Use - distribution in animals and plants:
 - Canadian Animal Health Institute, Impact Vet, commodity groups, PMRA
 - » Antimicrobial Use - distribution in humans:
 - PHAC - Centre for Communicable Diseases and Infection Control
 - » Targeted Studies :
 - UofGuelph, UofWaterloo, UofSask, UofMontreal, UofCalgary, UofLethbridge, UBC, AAFC, CSU, Texas A&M, Cornell, Oakridge National Lab, UofGlasgow



EXTRA SLIDES

Colección de información



- Fase de producción de interes: cerdos listos para el mercado
- Un muestreo/visita para colección de datos por cada rebaño por año
- Veterinarios distribuyen el muestreo de los rebaños durante el año calendario



Muestras fecales de los rebaños* se recopilan y se envían por medio del veterinario

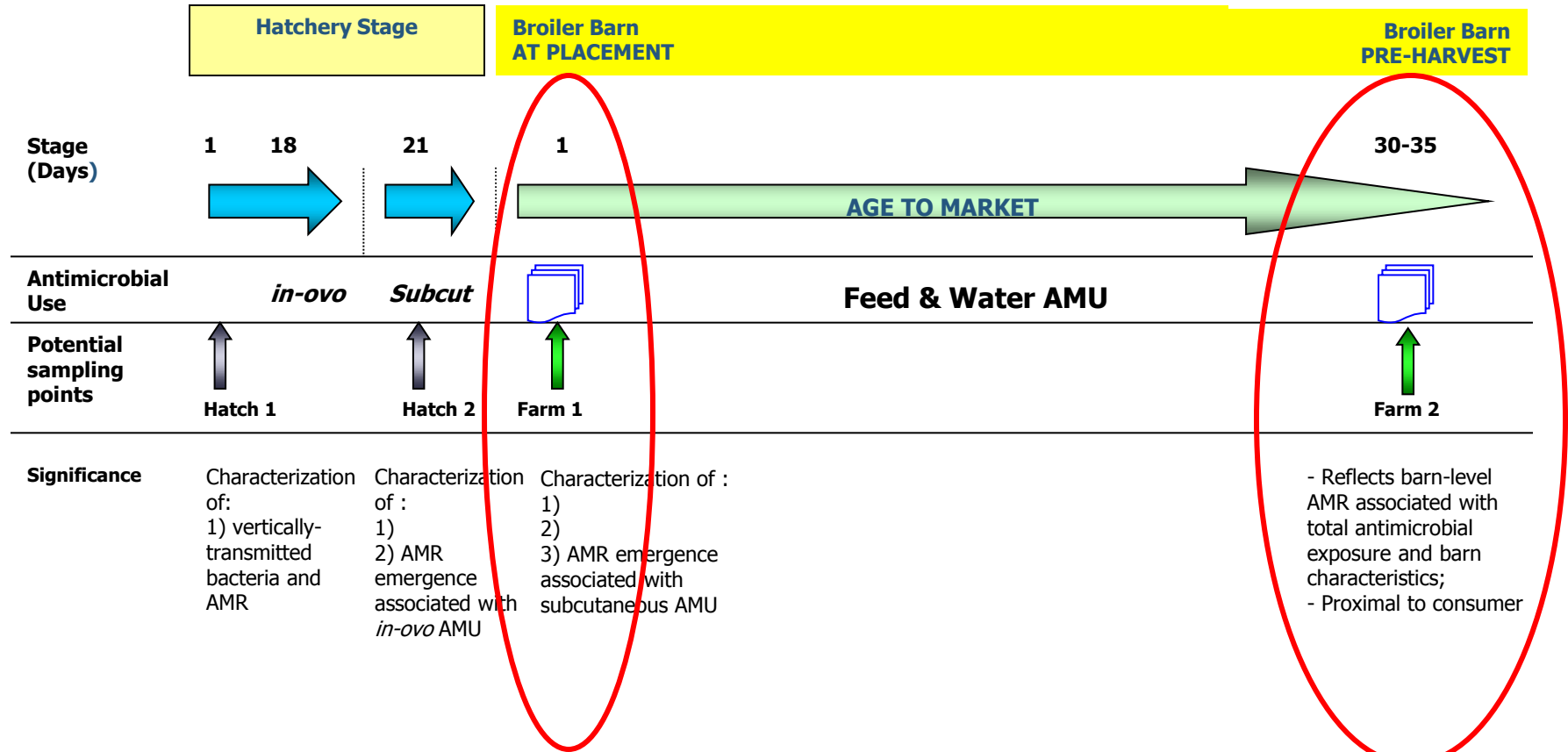
* *Close-To-Market*, pigs > 80 Kgs (175 Lbs)



Encuesta:

- Datos demográficos del rebaño/sitio
- Número de cerdos, muertes, al mercado
- Uso de antimicrobianos (comida, agua, inyecciones)
- Información de salud del animal

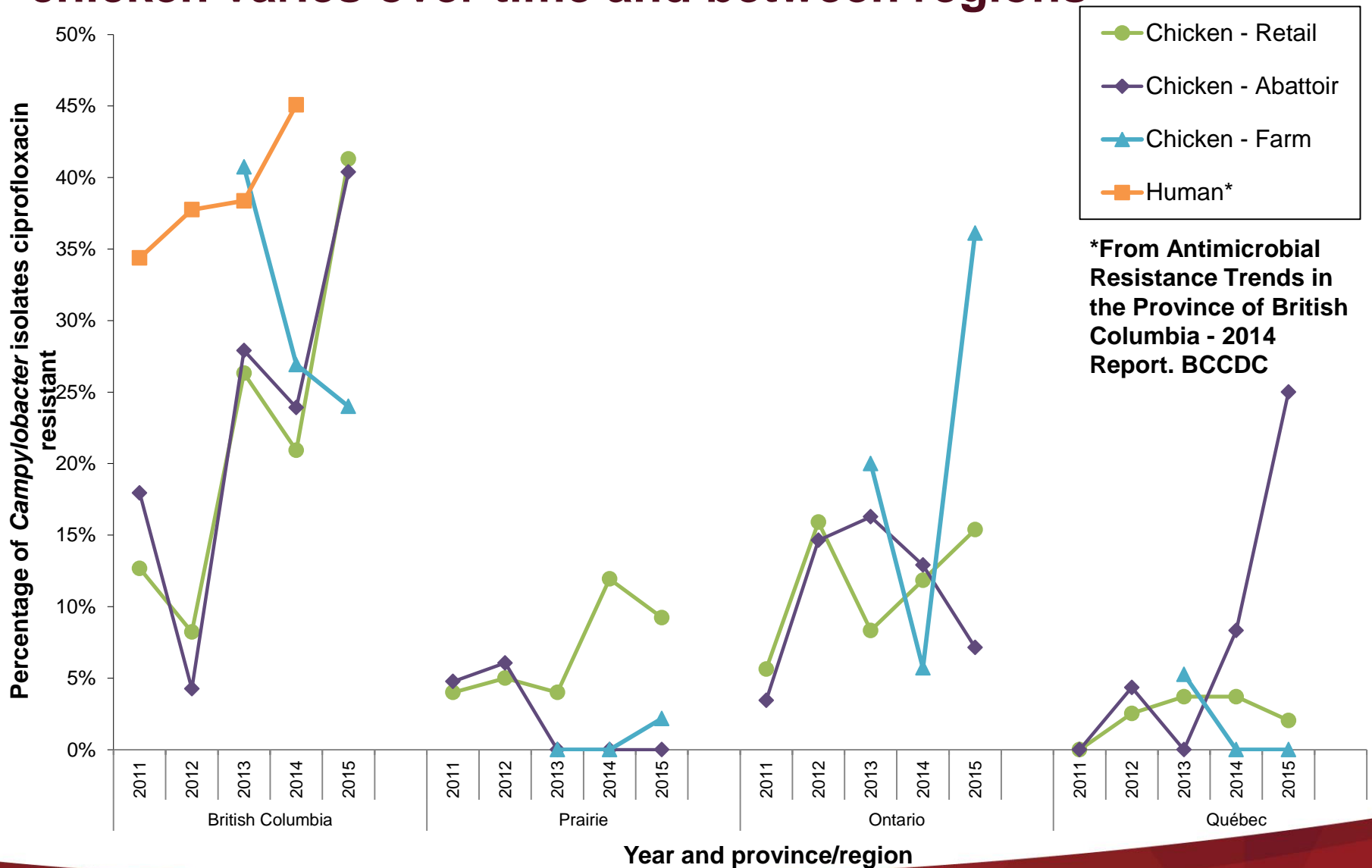
Colección de información



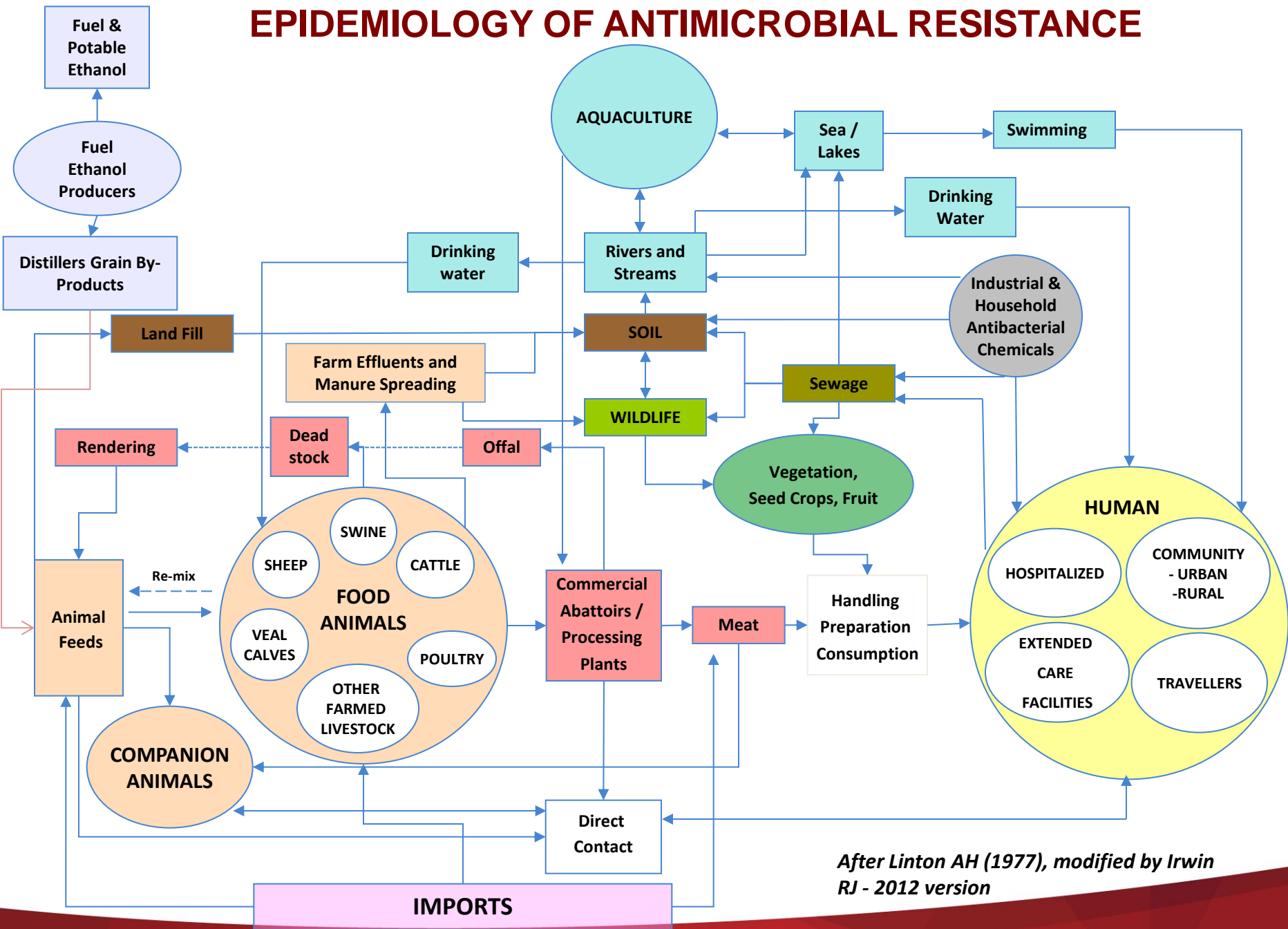
Ciprofloxacin-resistant *Campylobacter*

- **Resistance to ciprofloxacin in *Campylobacter* in chickens:**
 - Increased resistance in British Columbia chicken from abattoir and retail compared to 2014; reduced resistance at farm
 - Resistance on farm was higher in Ontario than British Columbia in 2015
- **No reported fluoroquinolone use in broiler chickens since 2013**
- **No approved products**
- **A high proportion of human *Campylobacter* cases from British Columbia resistant to fluoroquinolones**

Ciprofloxacin resistance in *Campylobacter* isolates from chicken varies over time and between regions

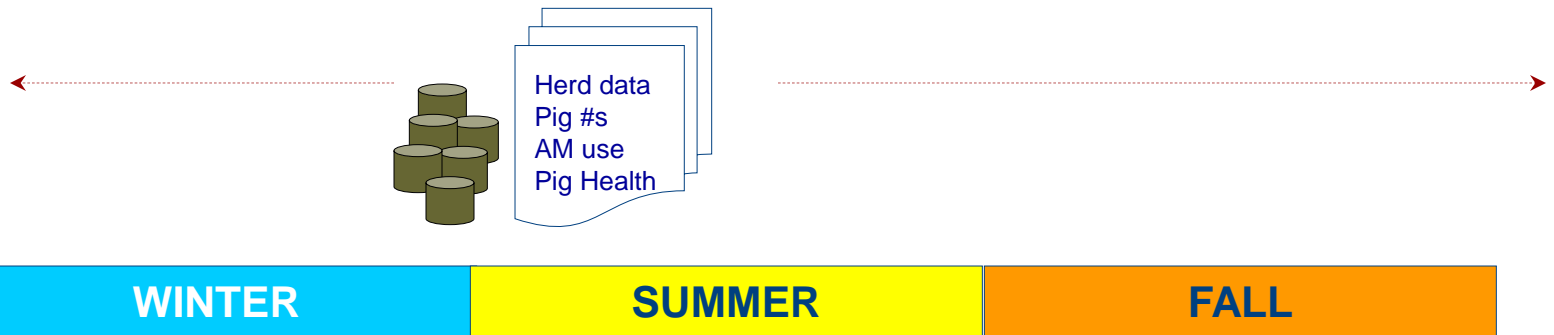


EPIDEMIOLOGY OF ANTIMICROBIAL RESISTANCE




After Linton AH (1977), modified by Irwin RJ - 2012 version

CIPARS Farm – Swine: Sampling & Data Collection



- Production phase of interest: Close-to-market **grower-finisher swine**
- One sampling/data collection visit per herd per year
- Veterinarians distribute sampling of herds over the calendar year

 Composite fecal samples from CTM* pens collected & submitted by the herd veterinarian



CTM* Questionnaire:

- Herd/site demographic data
- Number of pigs, mortalities, marketed
- **Antimicrobial use** data (Feed, Water, Inj.)
- Animal health data

* **CTM** = *Close-To-Market*, pigs > 80 Kgs (175 Lbs)

mcr-1 Methods

- Developed screen plate for colistin-R
 - Mueller Hinton, 2 mg/L colistin;
 - 1/10 dilution of 0.5 MacFarland dilution
 - Spot 2 ul on plate
 - validated on 100 *Enterobacteriaceae*

- Multiplex PCR
 - TEM, SHV, CTX, CMY, OXA-1
 - *mcr-1* and *mcr-2*

Extended-spectrum β -lactamase (ESBL) resistance from Retail

- CIPARS monitors for ESBLs using multiple approaches:
 - Routine surveillance & targeted sampling with selective media
- From 2014-2015 at retail:
 - 63 ESBL total – sample types varied:
 - Spices (n=7)
 - Chicken (n=6)
 - Turkey (n=2)
 - Pig – pork chops (n=3)
 - Ground beef (n=1)
 - Shrimp/prawns (n=27)
 - Clam/scallop/sea coconut/octopus (n=15)
 - Cuttlefish/salmon (n=2)
 - 32 isolates were confirmed as *E. coli* by whole genome sequencing (WGS)

Comparison of active/food chain and passive/clinical surveillance for detection of rare AMR profiles

- Active/Healthy Surveillance (AS) vs Passive/Clinical (PS)
- Chicken (*S. Heidelberg*); pigs (*S. Typhimurium*)
- No difference in prevalence of resistance to individual drugs between AS and PS **AMR: PS \approx AS**
- Prevalence of multidrug resistance (MDR) higher in PS isolates for both swine and chickens **MDR: PS $>$ AS**
- More unique AMR combinations (profiles) found in PS isolates for both swine and chickens **Diversity: PS $>$ AS**

Mather AE, Reeve R, Mellor DJ, Matthews L, Reid-Smith RJ, Dutil L, Haydon DT, Reid SW. Detection of Rare Antimicrobial Resistance Profiles by Active and Passive Surveillance Approaches. PLoS One. 2016 Jul 8;11(7):e0158515.

