Residu antibiotika pada pangan asal hewan dan pengujiannya

(Huda SD)

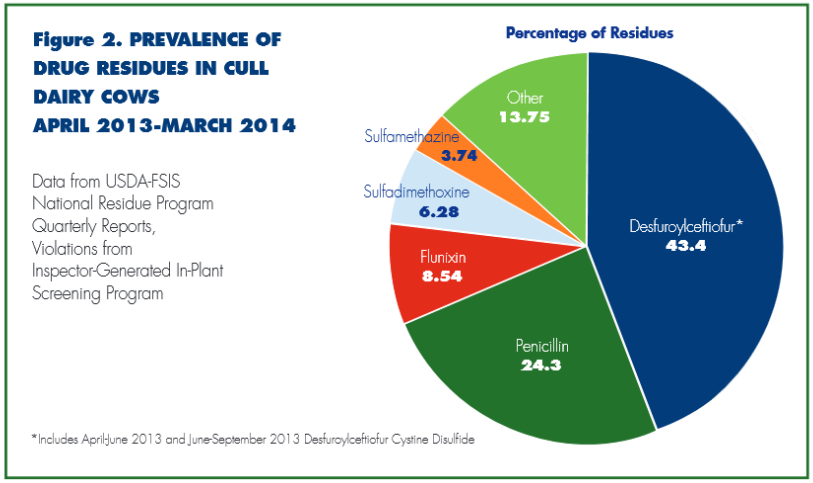
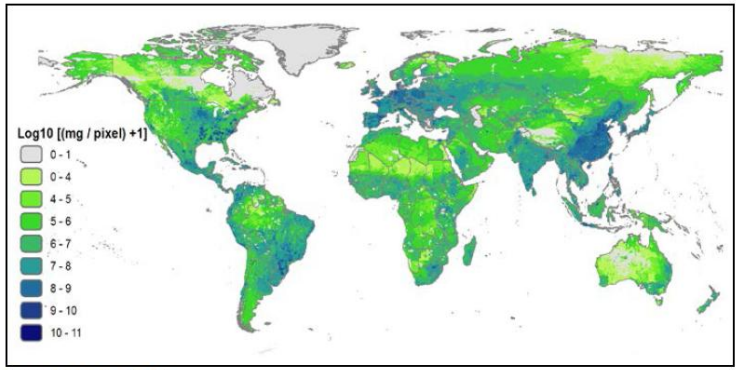


Figure 1 Global antimicrobial use in food animals (mg per 10km pixel)



from Van Boeckel et al., 2015

Bagian Farmakologi dan Toksikologi
Departemen Anatomi, Fisiologi dan Farmakologi
Fakultas Kedokteran Hewan, Institut Pertanian Bogor

Referensi – tersedia online

COMPASSION in world farming

ANTIBIOTICS IN FARM ANIMAL PRODUCTION

Public health and animal welfare

A Review of Antibiotic Use in Food Animals: Perspective, Policy, and Potential

Timothy F. Landers, RN, CNP, PhD[a]
Bevin Cohen, MPH[b]
Thomas E. Wittum, MS, PhD[c]
Elaine L. Larson, RN, PhD, FAAN, CIC[b]

ABSTRACT

Antibiotic use plays a major role in the emerging public health crisis of antibiotic resistance. Although the majority of antibiotic use occurs in agricultural settings, relatively little attention has been paid to how antibiotic use in farm animals contributes to the overall problem of antibiotic resistance. The aim of this review is to summarize literature on the role of antibiotics in the development of resistance and its risk to human health. We searched multiple databases to identify major lines of argument supporting the role of agricultural antibiotic use in the development of resistance and to summarize existing regulatory and policy documents. Several lines of reasoning support the conclusion that agricultural antibiotics are associated with resistance, yet most public policy is based on expert opinion and consensus. Finally, we propose strategies to address current gaps in knowledge.

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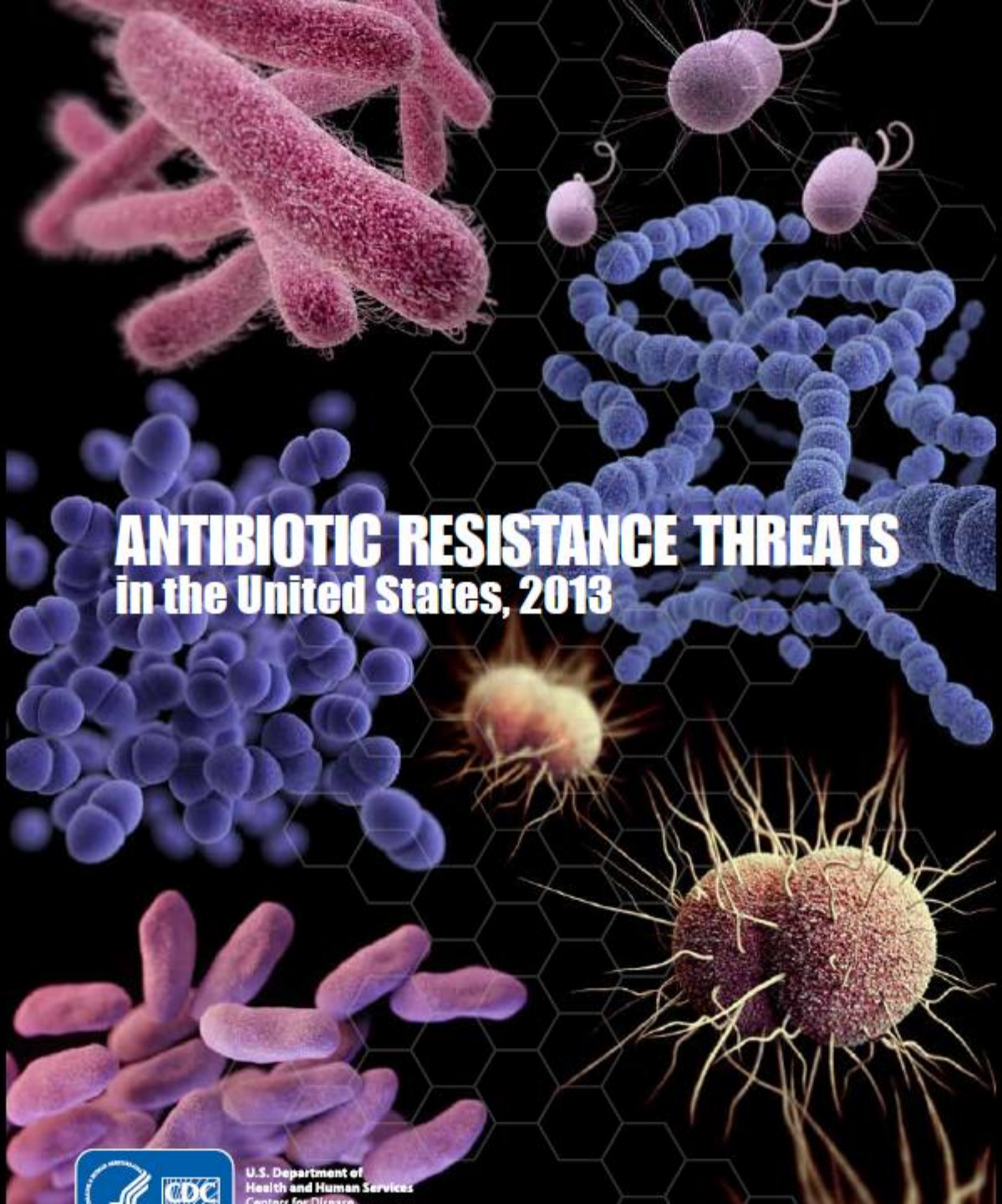
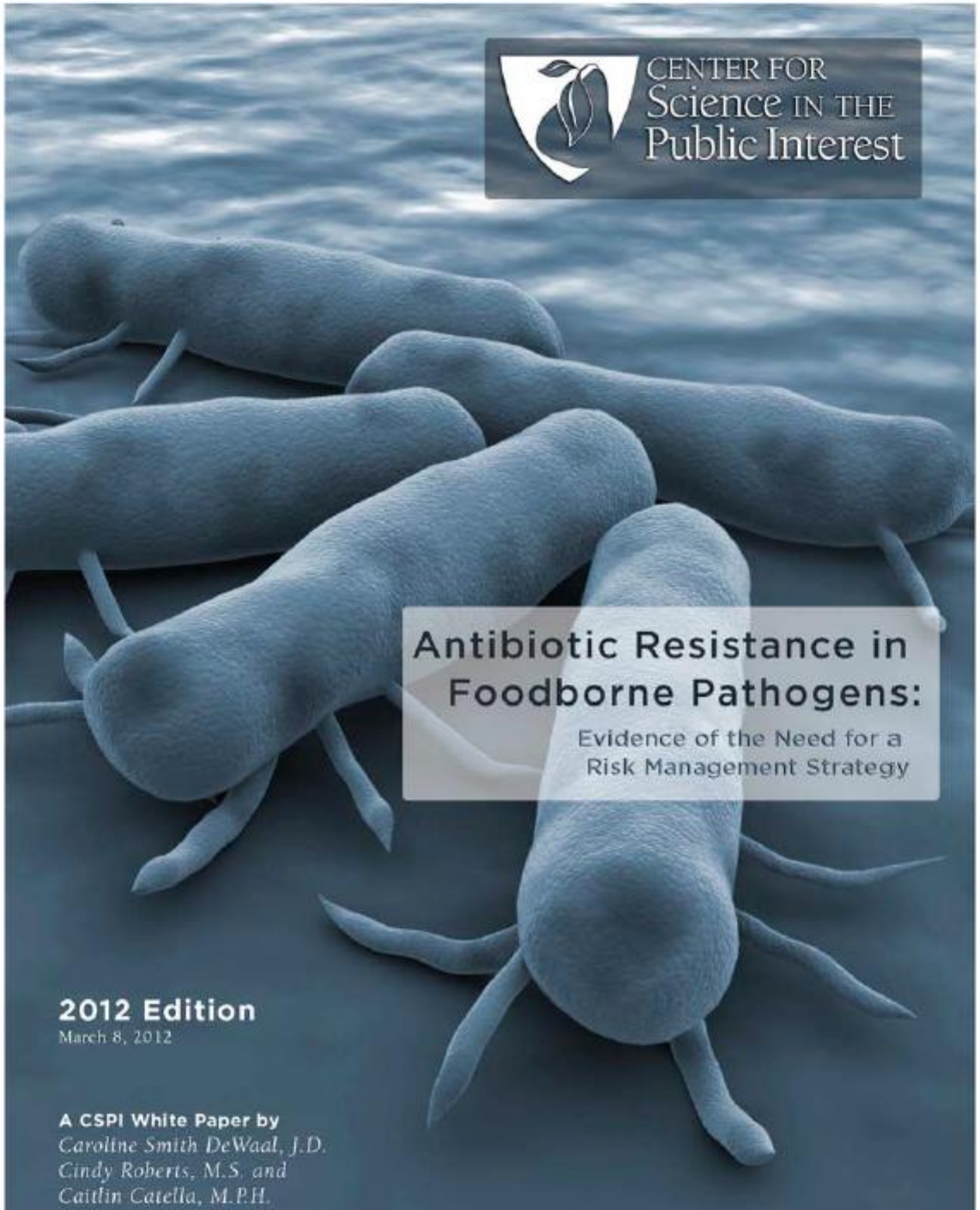
Antibiotic Use Guidelines for Companion Animal Practice



ANTIBIOTIC RESISTANCE THREATS
in the United States, 2013

U.S. Department of
Health and Human Services
Centers for Disease


CENTER FOR
Science IN THE
Public Interest
Antibiotic Resistance in
Foodborne Pathogens:
Evidence of the Need for a
Risk Management Strategy
2012 Edition
March 8, 2012
A CSPI White Paper by
Caroline Smith DeWaal, J.D.
Cindy Roberts, M.S. and
Caitlin Catella, M.P.H.

Raising Awareness for Prudent Use of Antibiotics in Food Animals

Position paper of the global Alliance for the Prudent Use of Antibiotics (APUA)

Prepared by Mary Wilson, M.D. and Melanie Tam

Presented at WHO Expert Meeting: Development of a Policy-oriented Guidance Booklet for the European Countries on Antimicrobial Resistance in a Food Safety Perspective
Rome, Italy, 11-12 November 2010

Residues of some veterinary drugs in animals and foods

FAO
FOOD AND
NUTRITION
PAPER

41/16

Monographs prepared by the
sixty-second meeting of the
Joint FAO/WHO Expert Committee
on Food Additives

Rome, 4–12 February 2004

WORLD HEALTH ORGANIZATION
FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS
Rome, 2004

UNITED STATES
National Residue Program for Meat, Poultry, and Egg Products

2014 Residue Sampling Plans

United States Department of Agriculture
Food Safety and Inspection Service
Office of Public Health Science

June 2014

FARMERS ASSURING RESPONSIBLE MANAGEMENT

NATIONAL DAIRY FARM PROGRAM™

Milk and Dairy Beef Drug Residue Prevention

Producer Manual of Best Management Practices

2015

Antimicrobial residues in foods of animal origin in Africa: public health risks

This paper (No. 10062014-00034-FR) has been peer-reviewed, accepted, edited, and corrected by authors. It has not yet been formatted for printing. It will be published in December 2014 in issue 33-3 of the *Scientific and Technical Review*

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Summary

The authors report on the current status of work on residues of veterinary medicinal products and, in particular, antimicrobial residues in foods of animal origin. This review focuses on residues of veterinary antimicrobials, antimicrobials used in livestock production, the concept of residues, and antimicrobial residues in foods of animal origin. Only one antimicrobial substance has been approved in the West African Economic and Monetary Union, compared with 16 substances in Benin and 56 in the European Union. The issue of antimicrobial residues in foods of animal origin has rarely been a serious concern in developing countries, in contrast to the situation in Europe. However, while the prevalence of veterinary drug residues in foods of animal origin is less than 1% in Europe, in some African

WHO Technical Report Series
988

Evaluation of certain veterinary drug residues in food

Seventy-eighth report of the
Joint FAO/WHO Expert Committee on
Food Additives

World Health Organization

CODEX ALIMENTARIUS
INTERNATIONAL FOOD STANDARDS

Food and Agriculture Organization of the United Nations
World Health Organization

E-mail: codex@fao.org - www.codexalimentarius.org

MAXIMUM RESIDUE LIMITS (MRLs) AND RISK MANAGEMENT RECOMMENDATIONS (RMRs) FOR RESIDUES OF VETERINARY DRUGS IN FOODS

CAC/MRL 2-2015

Updated as at the 38th Session of the Codex Alimentarius Commission (July 2015)

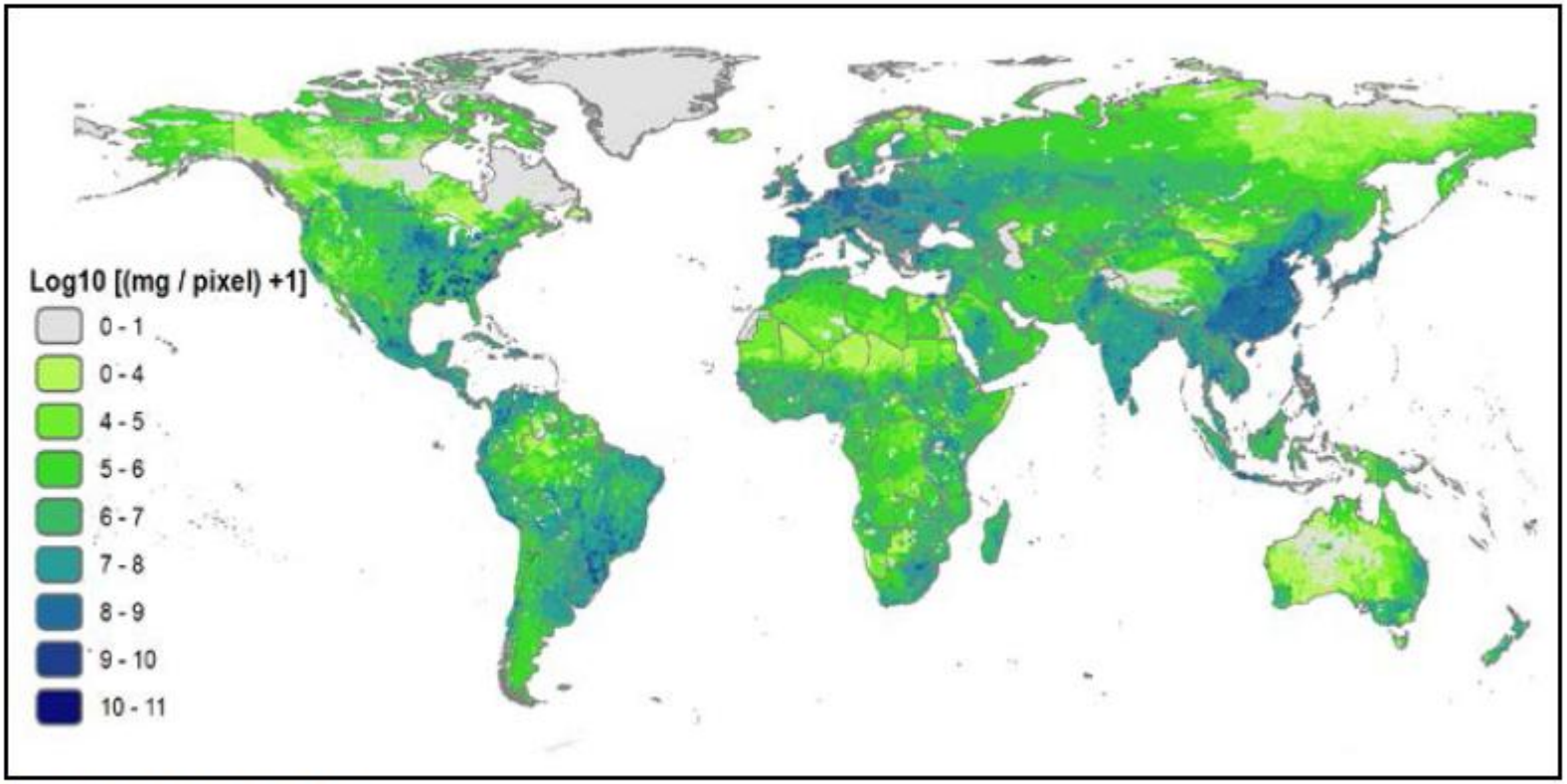
Antibiotika …

- Tidak terhindarkan → negara tropis adalah "surga" mikroorganisme

- Adalah obat yang **paling sering** digunakan dan disalahgunakan – use & abuse

Penggunaan antibiotika di dunia

Figure 1 Global antimicrobial use in food animals (mg per 10km pixel)



from Van Boeckel et al., 2015

Antibiotika…

- Penggunaan yang tepat membutuhkan keahlian:
  - medis → diagnosa & pemilihan jenis yang tepat – **tepat indikasi & tepat dosis**
  - paramedis → aplikasi & pengawasan
  - biologist & ecologist → analisis pengaruh pada hewan dan lingkungan
  - zoologist-peternakan&perikanan → manajerial pra, pasca
  - Epidemiologist → kajian efektivitas (farmakoepidemiologi/farmacovigilence) & analisis resiko

Antibiotika…

- Adalah satu dari sekian sediaan kemoterapetika

- Target kerjanya adalah kekhususan metabolisme organisme yang tidak terdapat pada induk semangnya

Pertimbangan seleksi antibiotika

- Faktor inang (host): usia, status imun, fungsi hati&ginjal
- Potensi toksisitas: ras tertentu tidak sensitif/toksik
- Kualitas obat ➔ konsentrasi obat pada lokasi infeksi
- Interaksi obat: synergis: bakterisid+bakterisid, antagonis: bakterisid+bakteriostatik
- Peraturan pemerintah setempat seputar residu
- **Patogen paling sering timbul**

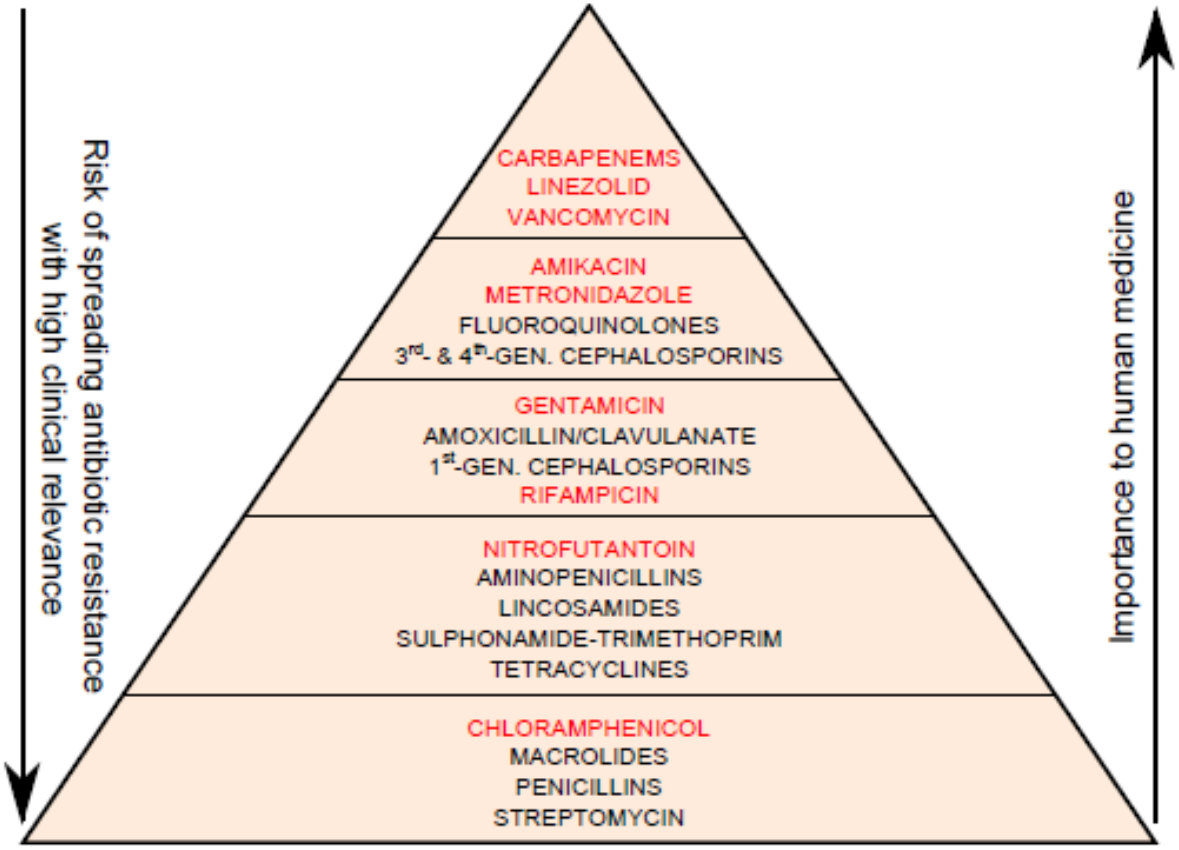


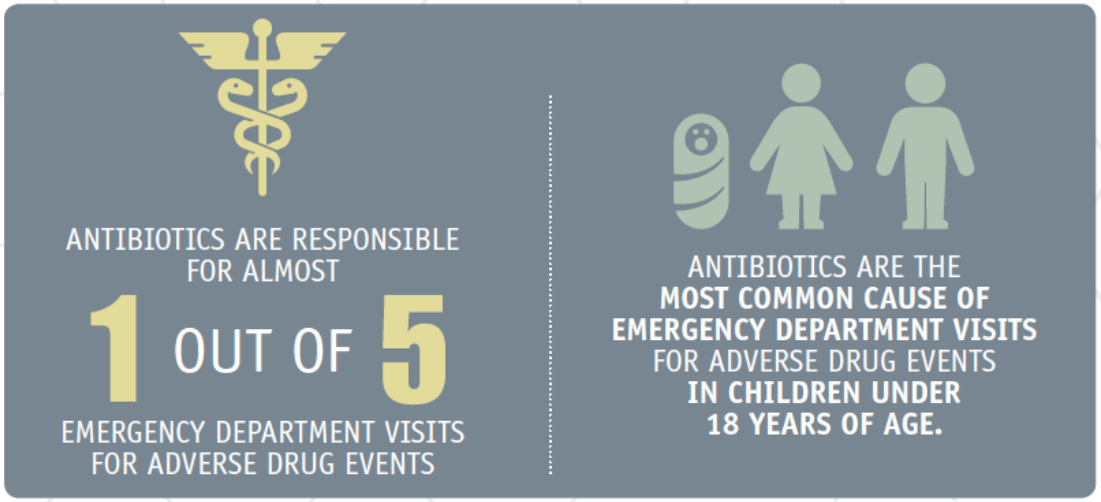
Figure 1.1.: Classification of systemic antibiotics based on clinical importance in human and veterinary medicine and the risk of spreading antibiotic resistance of high clinical relevance. Antibiotics with a particularly high risk for resistance and with few or no therapeutic alternatives in humans are placed in the top layer of the pyramid. Medications with a low risk of causing medically important antibiotic resistance are placed at the base of the pyramid. Antibiotics not licensed for use in companion animals are highlighted in red.

Efek merugikan akibat pemerian antibiotika

Pertanyaan …

Definisi

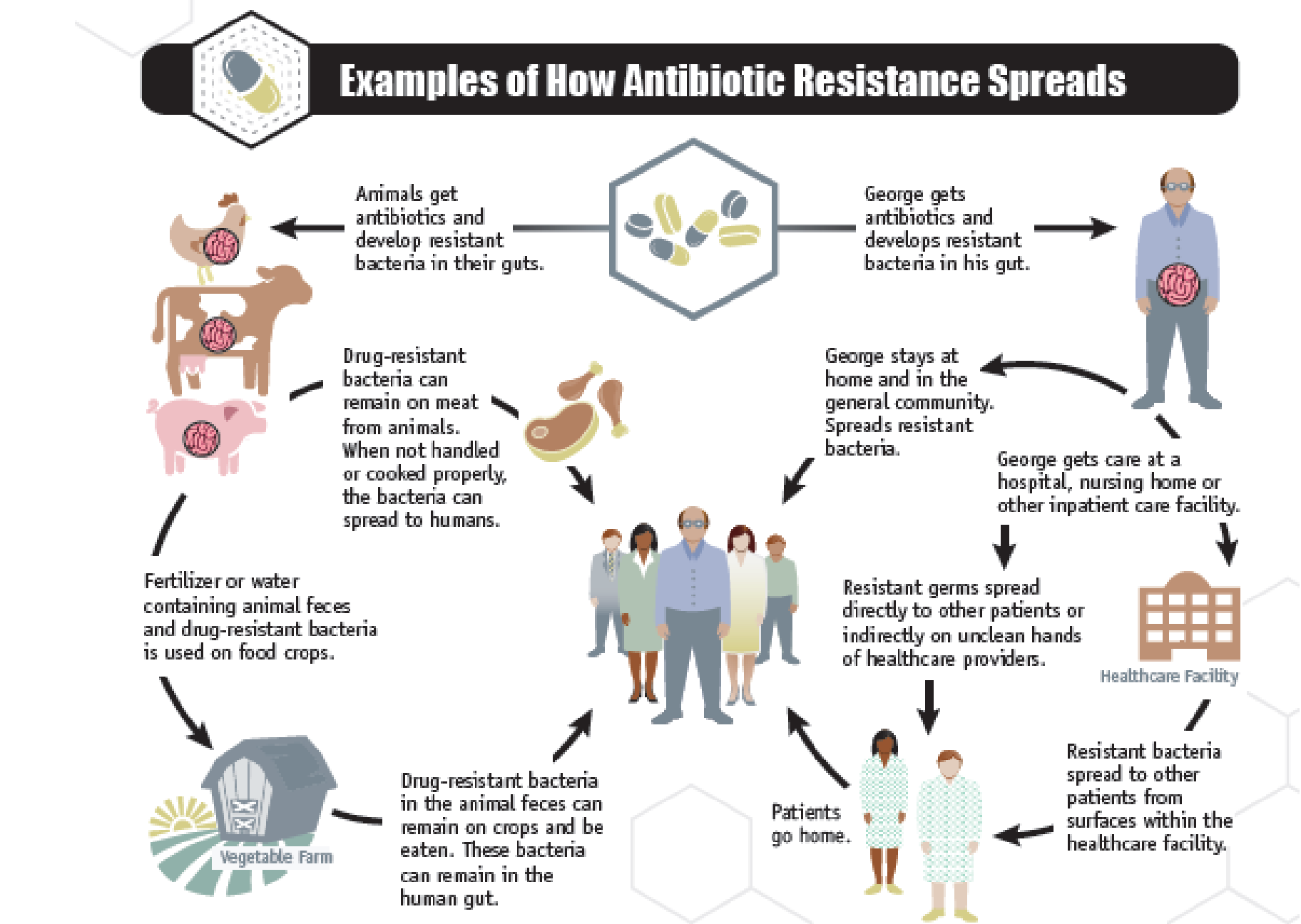
“ Residu suatu obat adalah bahan aktif dan eksipien atau sisa degradasi produk dan metabolit yang tertinggal di bahan pangan (Regulation No. 470/2009 of the European Parliament)”



Efek merugikan akibat residu

- Efek tidak langsung ➔ Resistensi
- Efek langsung ➔ Keracunan

Examples of How Antibiotic Resistance Spreads



Simply using antibiotics creates resistance. These drugs should only be used to treat infections.

CS239559

Ecological Impact of Antibiotic Use in Food Animals: The Flow of Antibiotic Resistance Bacteria

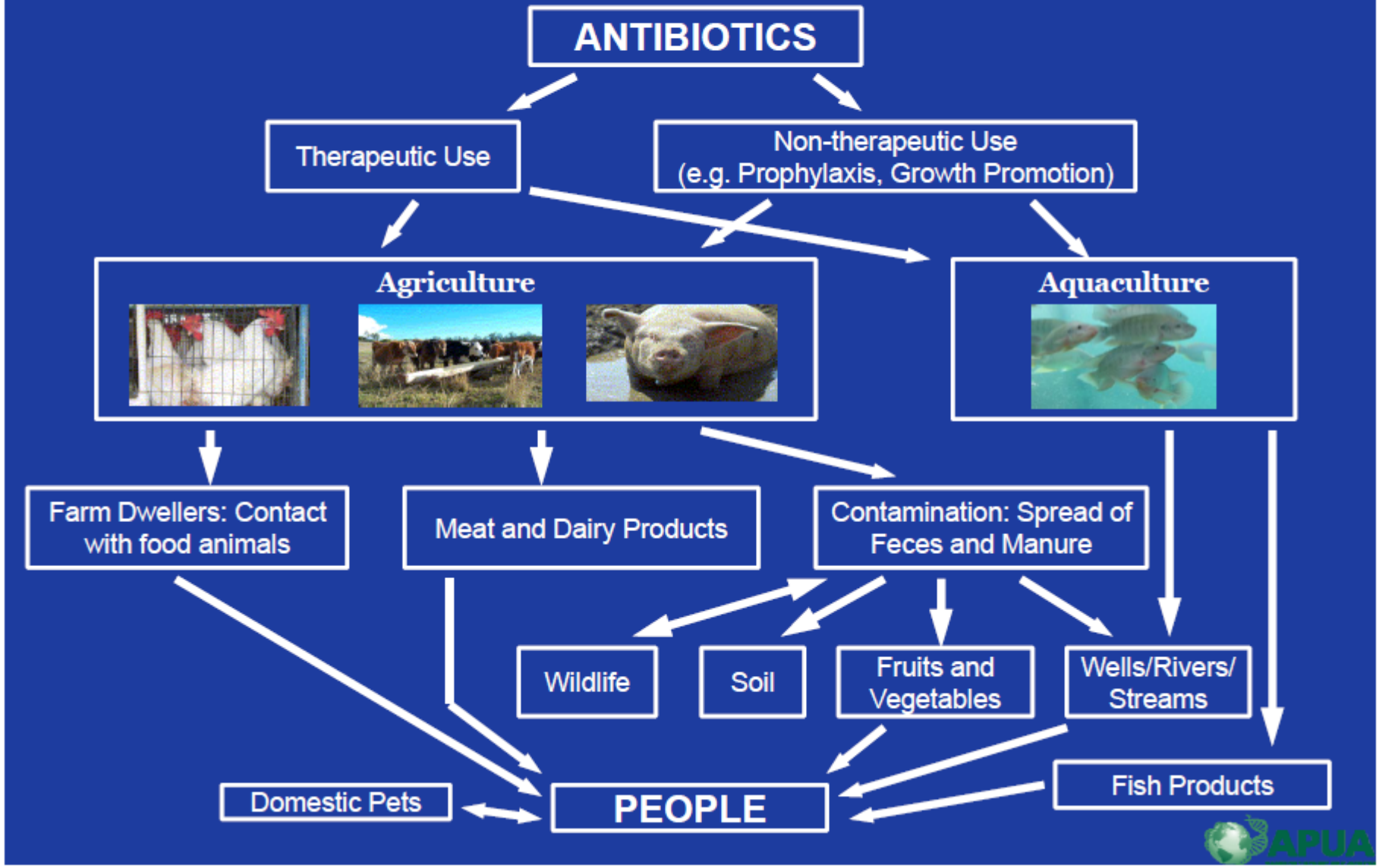


Table 1 Examples of how antibiotics used in animals can cause resistance to drugs used in people

ANTIBIOTIC CLASS	ANTIBIOTIC USED FOR FARM ANIMALS (BRAND NAME) AND TYPE OF USE	RELATED ANTIBIOTIC USED FOR HUMANS (BRAND NAME) AND TYPE OF USE	HUMAN HEALTH CONCERNS
Fluoroquinolones	***enrofloxacin (Baytril)*** Treatment of respiratory and alimentary tract infections in pigs and poultry (administered in poultry drinking water)	***ciprofloxacin (Cipro)*** Important for treating severe *Salmonella* and *Campylobacter* infections. Drug of choice for immediate ('empiric') treatment of *Salmonella* in adults	Use of enrofloxacin as prophylactic for chickens implicated in increasing resistance to Cipro
Cephalosporins 3rd generation (belong to beta-lactam class of antibiotics)	***Ceftiofur*** Treatment of bacterial infections by injection in cattle and pigs; in some countries, control of infection and mortality in day-old chicks	***cefotaxime, ceftriaxone*** Drugs of choice for treatment of severe *Salmonella* infections in young children	Use of ceftiofur implicated in development of resistance to 3rd generation cephalosporins
Streptogramins	***virginiamycin*** 'Growth promoter' (banned in EU from 1999)	***quinupristin-dalfopristin (Synercid)*** New antibiotic developed to treat resistant bacteria such as the 'superbug' vancomycin-resistant Enterococci (VRE) and hospital-acquired pneumonia	Use of virginiamycin for growth promotion was banned in the EU because its use could threaten effectiveness of Synercid in treating VRE and other

			dangerous infections
Glycopeptides	***avoparcin*** 'Growth promoter' (banned in EU from 1997)	***vancomycin*** Can be an antibiotic 'of last resort' for resistant *Staphylococcal* infections, including the hospital 'superbug' MRSA	The appearance of vancomycin-resistant *Entero cocci* (VRE) has been linked to use of avoparcin growth promoter. Concern that a vancomycin-resistant MRSA could develop
Macrolides	***spiramycin, tylosin*** 'Growth promotion' in pigs and occasionally in chickens (banned in EU for 'growth promotion' from 1999); tylosin still approved in EU for prevention, control and treatment of infections in pigs	***erythromycin*** Treatment of respiratory infections and food-borne infections such as *Campylobacter*; treatment of people who are allergic to penicillins	Bacteria which develop resistance to tylosin are often cross-resistant to erythromycin

"Pada hewan ternak, tindakan profilaktis antibiotika adalah **SUMBER UTAMA RESIDU & RESISTENSI PADA MANUSIA"**

Efek merugikan akibat residu

- Efek tidak langsung ➔ Resistensi

- Efek langsung ➔ Keracunan

Intoksikasi

- Transfer resistensi: bakteri resisten terminum ➔
  - Pengobatan terhadap kasus penyakit menjadi **TIDAK BERKHASIAT**
  - Superinfeksi

- Sulfonamid: karsinogenik & mutagenik

Intoksikasi

- Keracunan karena residu obat:
  - Basitrasin menyenbaban gangguan ginjal (jika termakan via residu)
  - Macrolides gangguan cerna (diare)
  - Carbadox and olaquindox: kerusakan adrenal → gangguan hormon & **DIABETES**

Intoksikasi

- Alergi: gejala kulit (kontak dermatitis) makrolida, basitrasin, quinolon

- Antibiotika & mikroflora normal: perubahan populasi bakteri Enterik & peningkatan populasi bakteri **patogen resisten**


Break..
Pertanyaan?
Prepare for the Uncertain.

Challenges

- Tuntutan masyarakat untuk pangan asal hewan yang **A**-**S**-U-H

- Sediaan di hewan yang sama atau satu golongan dengan manusia → **Dilarang di hewan**
  - Belum konsisten - DHS
  - Intoksikasi & residu
  - Obat terdaftar di manusia untuk hewan? Cerita beta agonis

Challenges

- Perkembangan antibiotika sebagai drug of choice
- Regulasi ➔ legalitas penggunaan obat untuk profilaksis ➔US OK,Eropa tidak, Asia sebagian besar OK, Indonesia tidak – feed additive vs medicated feed?
- Pelarangan profilaksis ➔ menaikkan metafilaksis
- (terlalu) terfokus pada unggas
- Assessment – regular monitoring

GREATER MILK PRODUCTION EFFICIENCY[1]* HAS A WAY OF ENERGIZING A DAIRY FARM.

Rumensin® gives your cows a boost of extra energy†—energy that can increase their milk production efficiency.[1]* To see how you can get the most out of dairy feed with Rumensin, contact your Elanco representative.

Acuan assessment

- Library standar harus ditingkatkan **berbadning lurus** dengan variasi drug of choices
- Metode assessment
- Monitoring reguler pada hewan & pada manusia (?)

Acuan assessment

- Library standar harus ditingkatkan **berbanding lurus** dengan variasi drug of choices
- Metode assessment
- Monitoring reguler pada hewan & pada manusia (?)

Obat veteriner

3 jenis obat veteriner

- Over the counter (OTC)
- Resep (Rx)
- Obat pada pakan

Diluar ketiga jenis obat tersebut → obat ekstra label → obat yang digunakan diluar ketentuan

Obat ekstra label – FDA AMDUCA*

1. Merubah dosis – menaikkan
2. Merubah rute (IV dijadikan IM, IM jadi SC dst)
3. Merubah frekuensi – menaikkan
4. Memberikan obat pd hewan target yg berbeda
5. Memberikan obat berbeda indikasi – beda bakteri beda obat
6. Memodifikasi waktu tunda obat
7. Mengganti banyaknya obat per injeksi per tempat
8. Mengganti durasi

(*Animal medicinal drug use clarification act - CFR Section 530.41(a)

Prohibited extra label for animal and human drugs

1) Chloramphenicol
2) Clenbuterol
3) Diethylstilbestrol (DES)
4) Dimetridazole
5) Ipronidazole
6) Other nitroimidazoles
7) Furazolidone
8) Nitrofurazone
9) Sulfonamide drugs in lactating dairy cattle (except approved use of sulfadimethoxine,
sulfabromomethazine, and sulfaethoxypyridazine)
10) Fluoroquinolones (examples ciprofloxin, enrofloxacin)
11) Glycopeptides
12) Phenylbutazone in female dairy cattle 20 months of age or older
13) Cephalosporins (not including cephapirin) in cattle, swine, chickens, or turkeys

CFR Section 530.41(a)

Obat yang **dilarang** untuk hewan produksi

- Chloramphenicol
- Clenbuterol
- Diethylstilbestrol (DES)
- Dipyrone
- Gentian violet
- Glycopeptides (example vancomycin)
- Nitrofurans (including topical use)
- Nitroimidazoles (including metronidazole)

Protect Your Farm with Charm

RESIDUE PREVENTION

Charm® Antibiotic and Aflatoxin Solutions:

Charm (SL) Safe Level Test: Beta-lactam results in 3 or 8 minutes. Charm tests are the industry quality standard.

Charm (SL) Aflatoxin Tests: Validated test to detect action level of concern and a NEW 3 minute visual test for farm use.

Charm ROSA® QUAD Tests: Four drug detections on a single test, customized to meet a variety of 12 different antibiotic families.

Broad Spectrum Inhibition: CowSide® II test for beta-lactams, sulfonimides, aminoglycosides, and tetracyclines is the most comprehensive inhibition test.

Live Animal Testing: KIS test for determining the status of antibiotics in an animal before market.

Contact Charm Sciences for residue concerns.

CHARM SCIENCES INC
659 Andover Street | Lawrence, MA 01843 | 1.978.687.9200 | info@charm.com | www.charm.com

USDA FSIS

- USDA FSIS (Food safety Inspection Service) – di Indonesia BPMSPH (?)
- Milk antibiotic residue testing target: grade A PMO (*Pasteurized Milk Ordinace)*
- Multiple screening test for bulk tank milk (LC-MS/MS)
- Multiple drug residue testing – RPH/slaughter house

  Sampling yang terjadwal dgn obyek random pada "healty appearing food animal"

Antibiotik target pemeriksaan

- Beta laktam: ampicillin, penicillin G, cloxacillin, cephapirin
- Sulfa: sulfamethazine, sulfadiazine, sulfadimethoxine, sulfathiazole, sulfaquinoxaline, sulfapyridine, sulfachloropyridazine, sulfamerazine
- Tetrasiklin: oxytetracycline, tetracycline, chlortetracycline, doxycycline
- Quinolon: sarafloxacin, enrofloxacin or ciprofloxacin,
- Misc: tylosin, tilmicosin, erythromycin, flunixin, bacitracin, thiabendazole, virginiamycin, and tripelennamine.

Figure 1. PERCENT OF BULK MILK TANKERS POSITIVE FOR ANTIBIOTIC RESIDUES, 1995–2013.

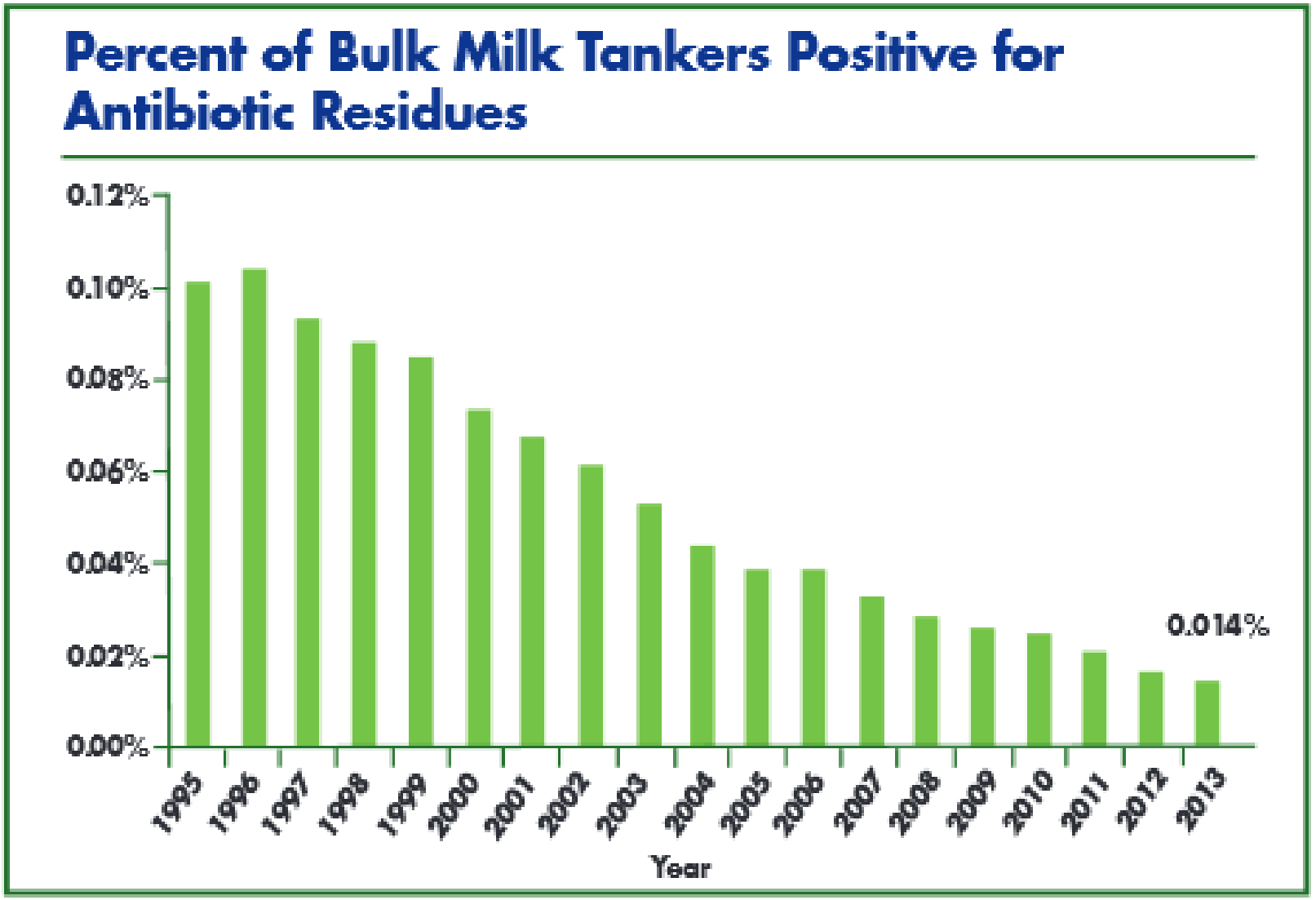
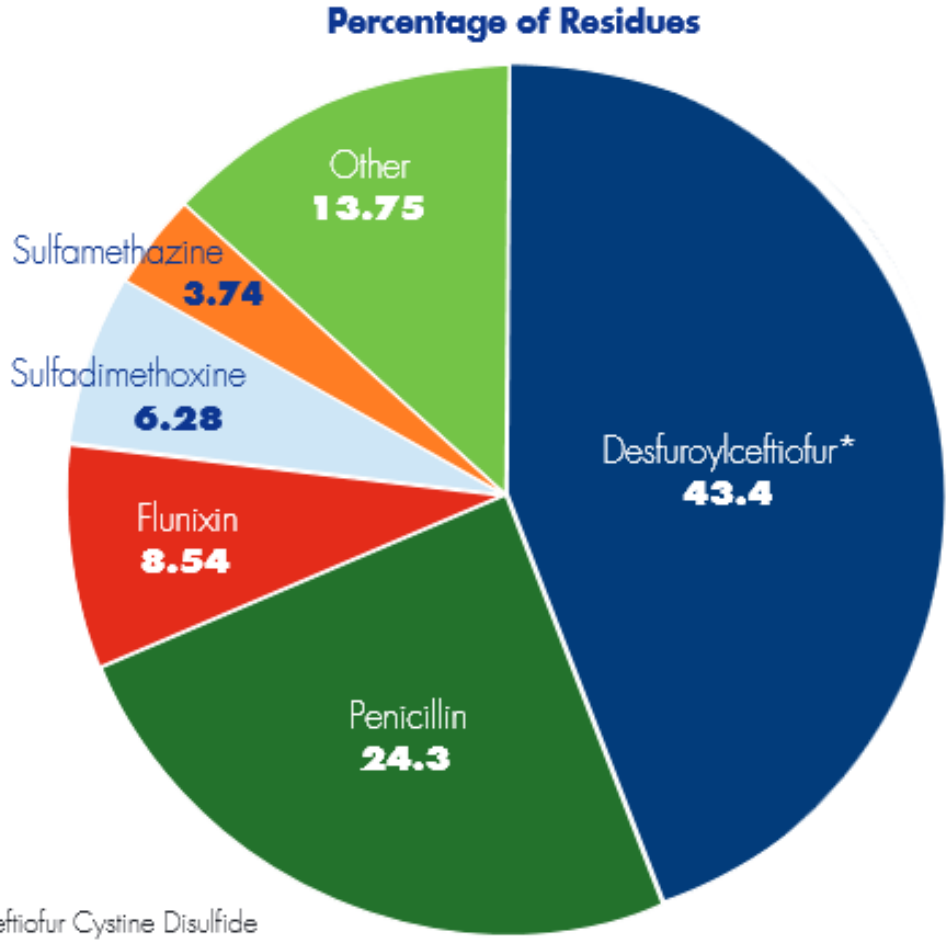


Figure 2. PREVALENCE OF DRUG RESIDUES IN CULL DAIRY COWS APRIL 2013-MARCH 2014

Data from USDA-FSIS National Residue Program Quarterly Reports, Violations from Inspector-Generated In-Plant Screening Program



*Includes April-June 2013 and June-September 2013 Desfuroylceftiofur Cystine Disulfide

Ceftiofur (also known as Ceftiflex®, Excede®, Excenel®, Naxcel®, Spectramast®)	- Using the withholding time for one product when using another. The withholding times for each product are different. - Not keeping accurate records to record the exact product given (Excede versus Excenel). - Using the drug in an unapproved route of administration. Excede is labeled to be given at the base or pinna of the ear only. Spectramast is the only ceftiofur product labeled for intramammary administration.Using these drugs in a route of administration not listed on the label is prohibited. - All products have a preslaughter withdrawal period, please consult prescribing veterinarian or manufacturer for withdrawal times.
Enrofloxacin (Baytril 100®)	- Extra-label use in food animals is prohibited. - Only labeled for non-lactating dairy animals twenty months of age or less and beef animals for pneumonia.*
Danofloxacin (A180™, Advocin™)	- Extra-label use in food animals is prohibited. - Only labeled for non-lactating dairy animals twenty months of age or less and beef animals for pneumonia.*
Florfenicol (Nuflor®)	- Sustained release has a longer withdrawal time. - Not approved for dairy cattle over 20 months of age. - No tolerance level for dairy cattle.
Flunixin (also known as Banamine®, Flumeglumine®, Flu-Nix™, Flunixin meglumine**, Prevail™)	- Using the drug in an unapproved route of administration such as intramuscular or subcutaneous. These drugs are only approved for intravenous administration. - Using another administration route results in extended withdrawal times, well beyond the labeled withholding time.
Gentamicin	- Use of gentamicin results in extended withdrawal times and therefore its use is discouraged by AVMA, AABP and AVC. - Use of gentamicin in lactating dairy cows for intramammary use is not recommended. - FARAD recommends not less than a TWO-YEAR withdrawal and, therefore, the use of this drug should not be considered.
Neomycin	- Not following withdrawal time on the bag. - Feeding medicated milk replacer to calves to be processed for slaughter. - Extra-label use of oral neomycin products.
Penicillin	- Increasing the dose without using an extended withdrawal period. - Increasing the frequency or duration of administration without using an extended withdrawal period. - Using the drug in a route of administration not approved, such as intramammary or subcutaneous. - Giving more than 10CC/injection site (as per label instructions).
Sulfas	- Using any sulfonamide product not labeled for lactating dairy cows is illegal. - Using a higher dose or frequency of administration will result in extended withdrawal times. - Inadvertently administering a sustained release product when intending to use a daily use product.
Tetracycline	- Single-site, large-volume injection through non-intravenous route. - Extra-label use such as uterine infusion to treat an infected post-partum uterus.

*Bovine respiratory disease (BRD); consult product label for actual indications.
**Due to the high risk of a violative residue, flunixin must only be used intravenously and not be given by either subcutaneous or intramuscular routes of administration.

2015 Codex alimentarius

Maximum Residue Limits (MRL)

Abamectin
Albendazole
Amoxicillin
Avylamycin
Azaperone
Benzylpenicillin/Procaine benzylpenicillin
Carazolol
Ceftiofur
Chlortetracycline/Oxytetracycline/Tetracycline
Clenbuterol
Closantel
Colistin
Cyfluthrin
Cyhalothrin
Cypermethrin and alpha-cypermethrin
Danofloxacin
Deltamethrin
Derquantel
Dexamethasone
Diclazuril
Dicyclanil
Dihydrostreptomycin/Streptomycin
Diminazene
Doramectin
Emamectin benzoate
Eprinomectin
Erythromycin
Estradiol-17beta
Febantel/Fenbendazole/Oxfendazole
Fluazuron
Flubendazole
Flumequine
Gentamicin
Imidocarb
Isometamidium
Ivermectin
Levamisole
Lincomycin
Melengestrol acetate
Monensin
Monepantel
Moxidectin
Narasin
Neomycin
Nicarbazin
Phoxim
Pirlimycin
Porcine somatotropin
Progesterone
Ractopamine
Sarafloxacin
Spectinomycin
Spiramycin
Sulfadimidine
Testosterone
Thiabendazole
Tilmicosin
Trenbolone acetate
Trichlorfon (Metrifonate)
Triclabendazole
Tylosin
Zeranol

Risk Management Recommendations (RMR) for Residues of Veterinary Drugs

Carbadox
Chloramphenicol
Chloropromazine
Dimetridazole
Furazolidone
Ipronidazole
Malachite Green
Metronidazole
Nitrofural
Olaquindox
Ronidazole
Stilbens

“Penting untuk membuat list obat yang dilarang tetapi lebih penting memperbaharui list tersebut secara berkala dan menerapkan **BEST MANAGEMENT PRACTICES** (Code for Federal Regulation, FDA 2004)”

Best management practices residue

1. Hubungan baik dokter hewan-peternak (klien)-hewan (pasien)
2. Hanya obat hewan yang diresepkan atau OTC yang diperbolehkan
3. Administrasikan obat secara tepat (tepat indikasi & tepat dosis)
4. Pencatatan pengobatan yang diberikan
5. Edukasi peternak & masyarakat seputar obat yang menimbulkan residu dan bahayanya
6. Penerapan uji skrining residu (positif palsu vs negatif palsu)
7. Hanya hewan sehat yang diperkenankan untuk dikonsumsi (parameter klinis umum, BCS)

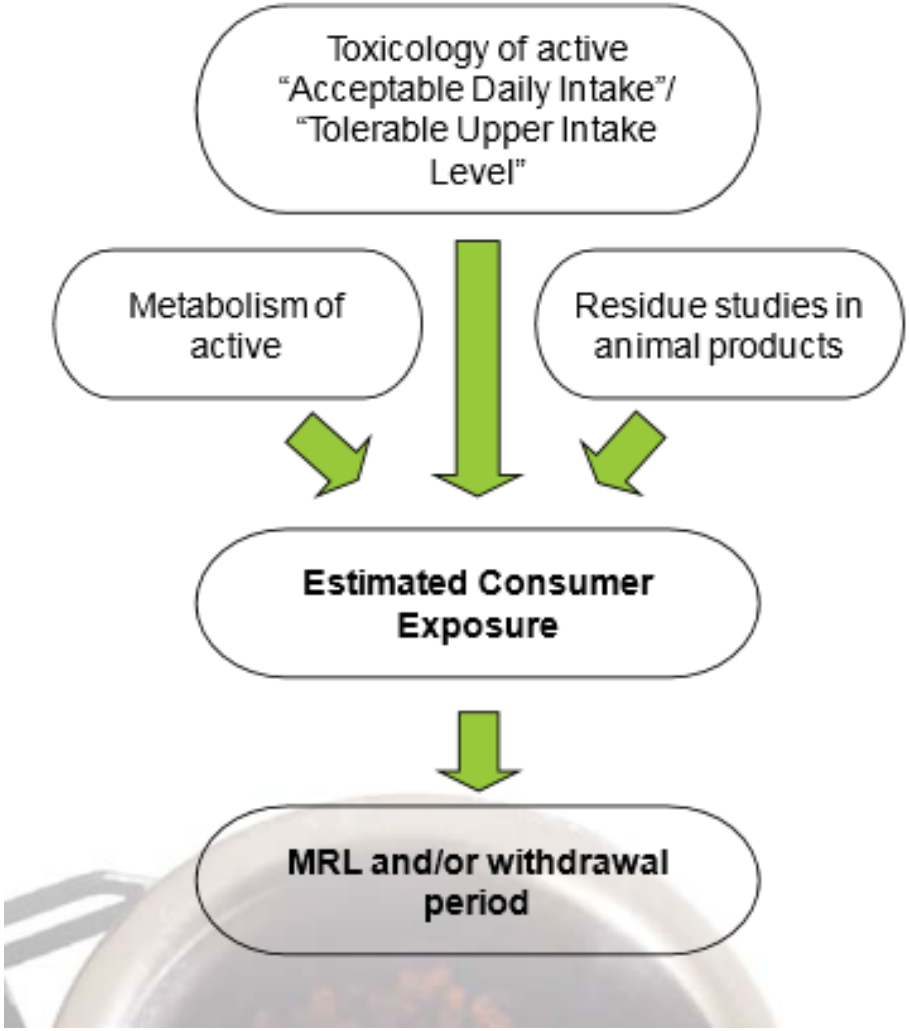
Manajemen dokumentasi pengobatan

- Dokumentasi (*recording*):
  - Tanggal treatment
  - Identitas hewan (spesies, ras, usia, jenis kelamin, dll)
  - Dosis
  - Rute pemberian & **perkiraan lamanya**
  - Personel yang mengaplikasikan
  - Obat yang digunakan
  - Durasi terapi (yang sesungguhnya)

Assessment residu

Animal product

Human exposure



Tantangan di Indonesia

- Obat yang dilarang – alasan vs regulasi vs kepentingan nasional
  - JOKOWI dengan “food sovereignty” berimplikasi pada percepatan proses pangan tetapi **tidak menimbang “modalities”** dalam monitoring keamanan pangan

- Pelarangan diatur sedemikian rupa sehingga “rigid – tidak mudah berubah untuk update”

- Obat yang diperbolehkan dan “**tetap masuk” – TIDAK ADA JUSTIFIKASI DAN KALKULASI**

Peoples at BPMSPH dan Kesmavet daerah…

"paling menderita" karena (sepertinya) bekerja di bagian hilir – terima obat yang ada dan menguji **yang seharusnya lebih** memiliki kewenangan untuk melakukan mediasi atau rekomendasi tindakan"

Assesment berkaitan dengan residu

Konsep residu menghasilkan definisi penting (sejak abad 20):

- *No oberved adverse effect level* (NOAEL)
- *Acceptable Daily Intake* (ADI)
- *Maximum residue limit* (MRL)
  - Antibiotika yang tidak dapat ditentukan MRL ➔ DILARANG (mis:kloramfenikol)

Residu

- Berhubungan kinetika obat (L-A-**D**-M-**E**)
  - Berhubungan dengan cara dan lama pemakaian
  - Berhubungan dengan waktu henti obat
- Penyalahgunaan obat

“kita semua sudah tahu pak dokteerrrr…”

Evaluasi keamanan residu obat veteriner (WHO, 2016)

- A risk-based decision-tree”

- Merupakan luaran dari joint meeting FA)-WHO bahwa obat veteriner dilarang apabila tidak memiliki MRL **dan ADI**

- Tahapan **“decision tree”** tersebut:
  - Preliminary risk assessment – identifikasi resiko – sampling & pengujian residu produk pangan
  - Penerapan kaidah toksikologi
  - ADI → assessmen respon akut

Contoh: Gentian violet

Summary and conclusions

Studies relevant to risk assessment

Species / study type (route)	Doses (mg/kg bw per day)	Critical end-point	NOAEL (mg/kg bw per day)	LOAEL (mg/kg bw per day)
Mouse				
Two-year study of toxicity and carcinogenicity (dietary)	Females: 0, 14.3, 35.7–39.3, 71.4	Erythropoiesis in spleen, atrophy of ovaries	–	14.3[a]
		Benign and malignant liver neoplasms (females)	–	**$BMDL_{10}$: 16.8***
Rat				
Two-year study of toxicity and carcinogenicity (dietary)	Males: 0, 30, 80, 160 Females: 0, 40, 100, 200	Increase in liver regeneration	–	30[a]
		Thyroid follicular cell adenocarcinoma (both sexes) and hepatocellular adenoma (males)	–	–
Three-generation study of reproductive toxicity, including developmental toxicity (dietary)	0, 5, 15, 30	Reproductive toxicity: No effects seen	30[b]	–
		Parental toxicity: Decreased body weight	15	30
		Offspring toxicity: Necrosis of thymus, focal dilatation of renal cortex and tubules, lowered red pulp haematopoietic cell proliferation in spleen	–	5[a]
Developmental toxicity study (gavage)	0, 2.5, 5, 10	Maternal toxicity: Reduced body weight gain, clinical signs	2.5	5
		Embryo and fetal toxicity: Increased hydroureter, hydronephrosis and short ribs	5	10
Rabbit				
Developmental toxicity study (gavage)	0, 0.5, 1, 2	Maternal toxicity: Increased mortality, decreased body weight gain, clinical signs	–	0.5[a]
		Embryo and fetal toxicity: Reduced fetal weight	–	0.5[a]

* **Pivotal study value** ***(11, 12)***
[a] Lowest dose tested.
[b] Highest dose tested.

ADI

The Committee concluded that it is inappropriate to set an ADI for gentian violet because it is genotoxic and carcinogenic.

MRLs

MRLs for gentian violet and leucogentian violet could not be recommended by the Committee, as no ADI was established and there is a lack of residue data.

Residue risk assesment

Low Risk
Animal history is documented, recorded and available.

❑ Animal never treated with drugs.

OR-

❑ Single drug administration of lactating/ non-lactating animal approved drug – AND
Followed drug label information for dose, route of administration, duration of therapy and withholding time.

OR-

❑ Veterinary oversight of the use of drugs in an extra-label manner.

High Risk
Animal is displaying lameness, injection sites, surgical evidence or looks sick – AND any of the below apply:

❑ History of animal treatment not documented or not communicated to person sending cow to market.

❑ Route of administration that was used is not as prescribed on the label.

❑ Multiple drug administration without veterinary oversight.

❑ Drug not approved for animal status, e.g. lactating.

❑ Doses or withholding times not followed or unknown.

❑ Duration of therapy not followed.

If any of the above high risk attributes exist, consult pharmaceutical, veterinary or screening test experts to determine status of animal before offered for sale – **When in doubt hold it out!**

Indonesia ??

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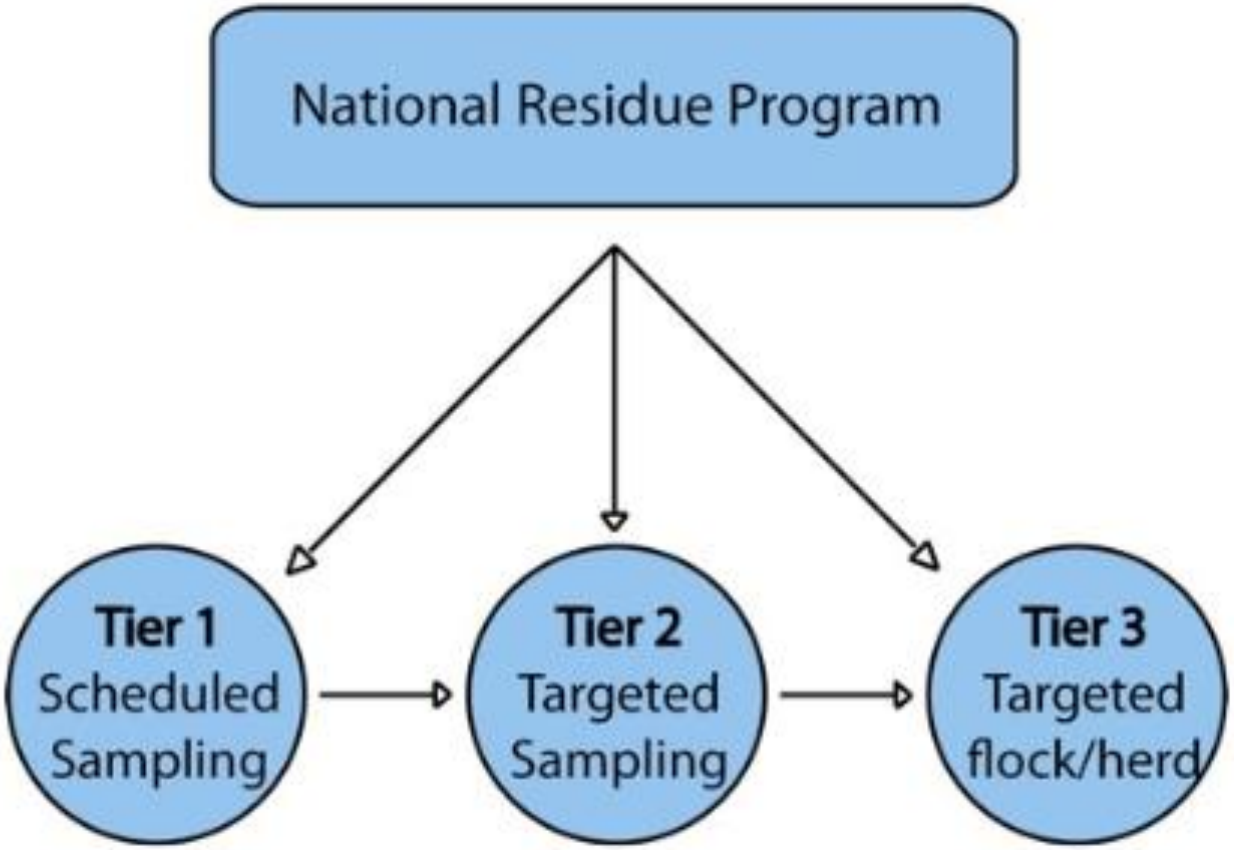
National Residue Program
Tier 1
Scheduled
Sampling
Tier 2
Targeted
Sampling
Tier 3
Targeted
flock/herd

“Rule of thumb” pengujian

- Rapid test – sensitivitas tinggi, spesifisitas tinggi → positif palsu
  - Uji analitik – pewarnaan – umumnya memiliki batas ambang deteksi yang tinggi – analitik – menghasilkan negatif palsu → pertimbangan u skrining?

- Confirmatory test – spesifisitas tinggi, sensitivitas tidak menjadi prioritas → negatif palsu

- Gold standar → sensitiv dan spesifik

- Di BPMSPH? Di Lab Kesmavet daerah? Tupoksi vs pengadaan ☺

Kesimpulan - untuk

- Up date “library” standar antibiotik
- Up date metode yang valid dan terstandar
- Penguatan monitoring & pencatatan
- Penerapan “best management practices”
- Penguatan peran kelembagaan

Sekian & terima kasih