COLLEGE OF VETERINARY MEDICINE

# Evaluation of Anthelmintic Resistance in OK Beef Cattle Herds

## Assessment of Composite Fecal Sampling for Herd Level Fecal Egg Count Reduction Testing

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# Objectives

- Investigate the prevalence of anthelmintic resistance in Oklahoma beef cow-calf herds via fecal egg count reduction testing

- Evaluate the use of composite fecal samples for detection of anthelmintic resistance at the herd level

- *Study was internally funded through OSU CVM*

# Fecal Egg Count Reduction Test (FECRT)

- How does it work
  - Collect fecal samples prior to treatment (~5 grams)
    - Send to lab for fecal egg count (FEC)
  - Collect fecal sample from same animals in 14-21 days
    - Send to lab for FEC
  - Examine the % reduction in egg shedding between pre- and post treatment samples
  - % reduction less than 90% indicates resistance

# Fecal Egg Count Reduction Test (FECRT)

- Limitations
  - Consistent lab methods are critical
  - Variable egg shedding between and within animals
  - Anthelmintic may suppress egg shedding but not kill the worms
  - Does not determine the species of parasite
  - Cost and labor intensive
    - Current OADDL price list: $25/sample

- **Currently the only way to assess anthelmintic efficacy**

# Background

- Anthelmintic resistance reported in weaned calves
  - Gasbarre et al. *Vet Parasitol* 2009
  - Gasbarre et al. *Vet Parasitol* 2009
  - Edmonds et al. *Vet Parasitol* 2010

- NAHMS Beef Cow-Calf Survey 2007-2008
  - Gasbarre et al. *Can J Vet Res* 2015
    - 33% of participating herds from the southeastern US had evidence of resistance
    - 2 of 4 herds from OK had evidence of resistance

# Background

- One report of FECR testing using composite samples **(George et al. *Vet Parasitol* 2017)**
  - Compared testing composite samples to testing individual samples
  - Compared results in 14 different groups of cattle with a wide range of FEC
  - **95.9% agreement for FECR% between individual and composite samples**
  - **Reduced FEC required by 79%**

# Materials and Methods

- Recruited beef cow-calf herds from around the state
  - Submitted pre and post-treatment (14 days) fecal samples
  - Target of 20 calves per herd
  - Herds encouraged to follow standard parasite control practices
    - Study did not dictate products used, timing, calf selection etc
    - Did ask producers to sample the same calves pre and post treatment
  - Producers asked to submit short survey regarding herd management practices

# Materials and Methods

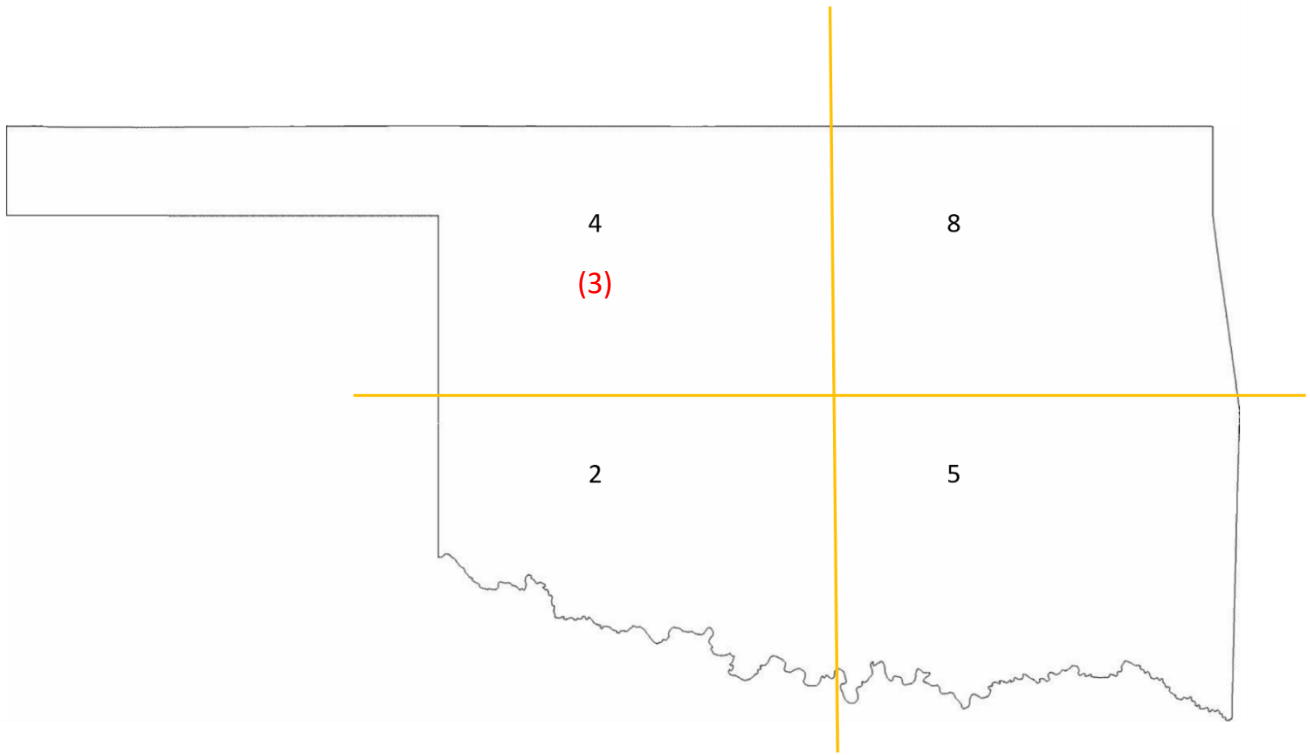
- Fecal Egg Count
  - Wisconsin method
  - Limit of detection of 1 egg per gram (EPG)
- Composite samples
  - 1 gram from each animal to create composite sample
  - Wisconsin method on composite sample
- Inclusion criteria
  - Minimum of 25 EPG in pretreatment sample for inclusion in final analysis
  - Applied at the individual animal level
- FEC Reduction %
  - FECR% = [1-arithmetic mean post treatment/arithmetic mean pretreatment)] x 100
  - FECR% < 90% = resistance

# Results - Animals

- 19 sample sets submitted
  - 17 herds represented (2 herds submitted two sample sets)
  - 16 sample sets included in the final analysis
    - 3 excluded due to pretreatment FEC <25 EPG
- 10-29 calves per sample set
  - Individual calves excluded for FEC <25 EPG ranged from 0-10 per set
  - Final calf numbers ranged from 8-24 calves per sample set
- 13 composite samples included in final analysis
  - One not performed, 5 had pretreatment FEC <25 EPG

# Results - Geographic distribution

- Northeast – 8
- Southeast – 5
- Southwest – 2
- Northwest – 4

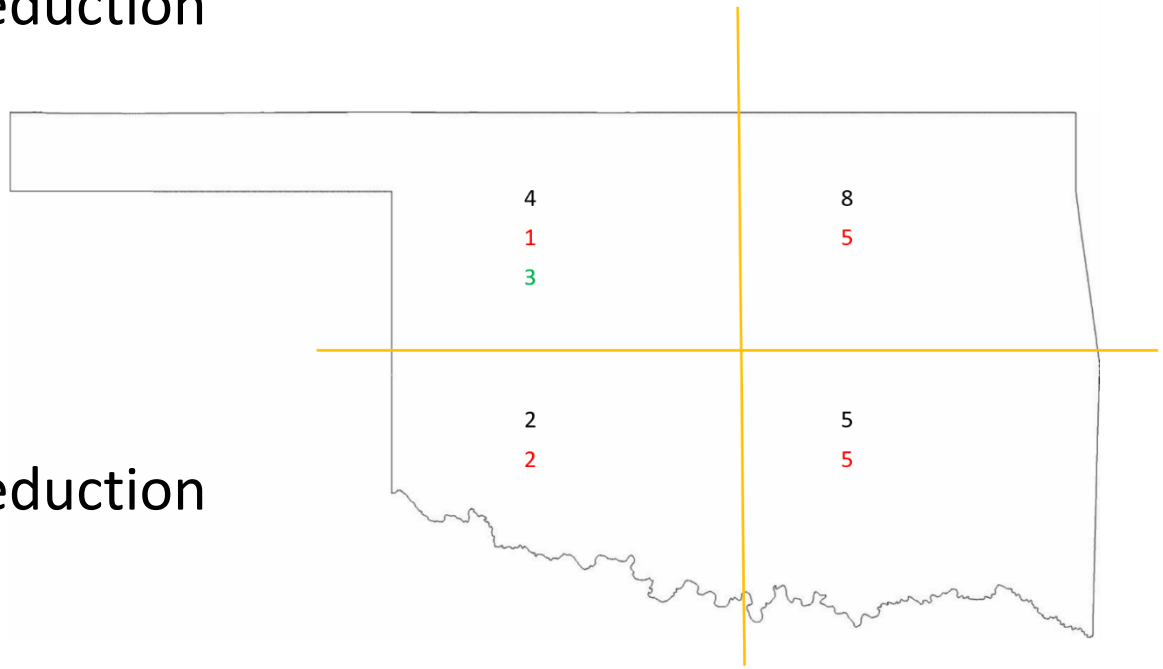


# Results - Herd Management

- Operation type
  - Commercial – 12
  - Seedstock – 2
  - Combination – 2
- Grazing management
  - Continuous grazing – 7
  - Rotational grazing – 7
  - Combination – 2
- Pasture type
  - Native grass – 4
  - Improved pasture – 7
  - Combination – 5
- Adults dewormed
  - Yes – 12
  - No- 1
  - Unknown – 3
- Weigh before dosing
  - Yes – 7
  - No – 9
- Anthelmintic product used
  - Injectable – 5
  - Pour-on – 7
  - Oral – 4

# Results – Fecal Egg Count Reduction

- Arithmetic means of individual samples
  - 13 of 16 (81%) failed to achieve >90% reduction
    - % reduction range - -46% - 72%
  - 3 of 16 (19%) achieved >90% reduction
    - % reduction all >99%




- Composite samples
  - 11 of 13 (85%) failed to achieve >90% reduction
  - 2 of 13 (15%) achieved >90% reduction

- Perfect concordance between arithmetic mean of individual samples and composite samples for resistance at the herd level

# Results – Anthelmintics Represented

| Anthelmintic Product | % Reduction |
|---|---|
| Dectomax Inj (2) | 11%, 19% |
| Dectomax PO (4) | -0.8%, 60%, 35%, 68% |
| Cydection PO (5) | 56%, 55% (3 herds excluded due to low FEC) |
| Noromectin Inj (2) | 33%, 25% |
| Ivermax Inj (1) | 72% |
| Bimection PO (1) | -46% |
| Safeguard Drench (3) | 99%, 99.9%, 99.5% |
| Valbazen Drench (1) | 63% |

# Results - Herd Management (Resistance/Total)

- Operation type
  - Commercial – 12 (9/12)
  - Seedstock – 2 (2/2)
  - Combination – 2 (2/2)
- Grazing management
  - Continuous grazing – 7 (6/7)
  - Rotational grazing – 7 (5/7)
  - Combination – 2 (2/2)
- Pasture type
  - Native grass – 4 (2/4)
  - Improved pasture – 7 (6/7)
  - Combination – 5 (5/5)
- Adults dewormed
  - Yes – 12 (9/12)
  - No- 1 (1/1)
  - Unknown – 3 (3/3)
- Weigh before dosing
  - Yes – 7 (4/7)
  - No – 9 (9/9)
- Anthelmintic product used
  - Injectable – 5 (5/5)
  - Pour-on – 7 (7/7)
  - Oral – 4 (1/4)

# Discussion

- Broad survey of OK beef cow-calf herds
  - Geography
  - Operation type
  - Pasture type
  - Grazing management
  - Type of anthelmintic product used

# Discussion

- “Apparent” resistance appears to be widespread among OK cow-calf operations
  - Apparent resistance
    - Uncontrolled factors may have influenced results
    - 4 of 7 herds that weighed prior to treatment still had evidence of resistance
  - Apparent resistance was not isolated to a particular geographic region, herd type, pasture type, grazing management strategy or anthelmintic class/product
    - Unable to determine influence of these factors due small numbers and overall poor anthelmintic performance

# Discussion

- Study was not design to compare anthelmintic products to each other

- Fenbendazole was a novel product in the herds in this study
  - Two herds had used injectable ivermectin for several years
    - Tested 2 sets of calves, ivermectin was not effective, fenbendazole was effective
  - One herd had started switching to fenbendazole within the last year
  - Other products may have been as effective if used under the same circumstances

# Discussion

- Composite sampling correctly classified all herds
  - When compared to arithmetic means of individual samples
  - George et al. found similar results (George et al. *Vet Parasitol* 2017)

  - More work is needed but composite sampling looks promising
    - May significantly reduce the costs of testing and increase interest by producers

# Limitations

- Small overall numbers
- Influence of uncontrolled factors is unknown
- Influence of low pretreatment FEC in some animals/composite samples is unknown

# Moving forward…

- No introduction of new anthelmintic compounds in many years
  - New product recently released – combination of existing products
- Must find other solutions to combat emerging resistance
- Goal should be suppression of parasites below an economic threshold while minimizing selection pressure for the development of resistance

# Strategies to reduce resistance

- Low hanging fruit….
  - Dose correctly
    - Weigh animals if possible
    - Dose to heaviest weight if estimating
    - If using pour-on, apply according to directions
  - Administer strategically
    - Time anthelmintic treatment to minimize pasture contamination
    - Avoid treating and immediately placing on clean pasture
  - Use products for intended purpose only

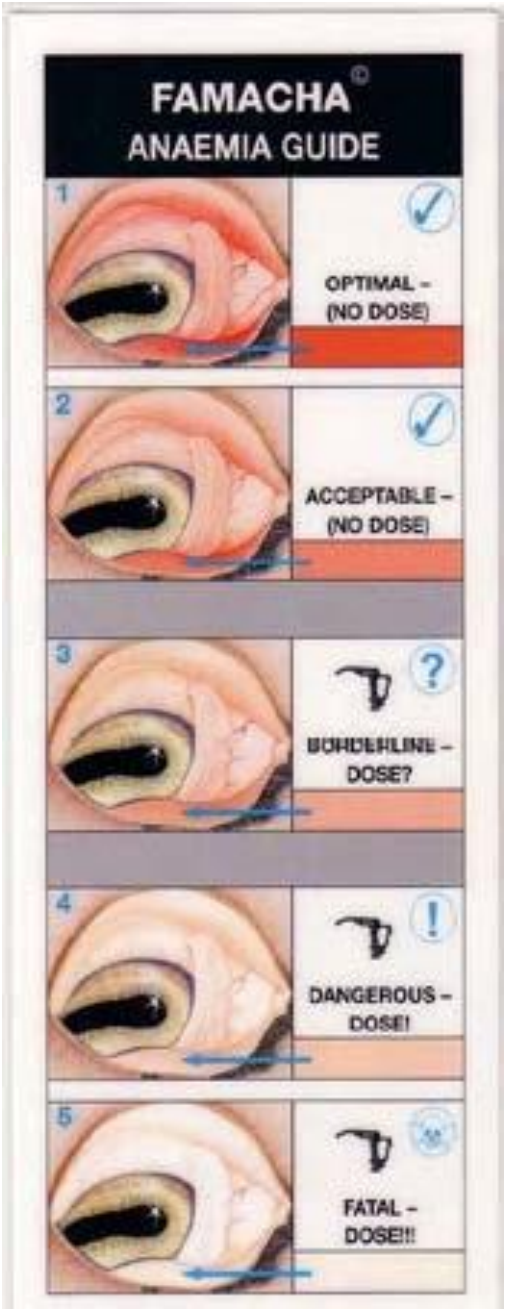
# Strategies to reduce resistance

- **Refugia**
  - Proportion of parasite population not selected for resistance via anthelmintic exposure
    - Population of parasites in animals that are not treated
    - Developmental stages of parasites not effected by treatment
    - Free-living population of parasites on the pasture
  - **Maintaining refugia avoids the concentration of resistant genotypes in the parasite population**

  - Targeted selective treatment
    - Treating animals with the highest parasite loads while leaving others untreated
    - No clearly established method for application to cattle
    - FAMACHA® system in sheep and goats

# Strategies to reduce resistance

- Refugia
  - FAMACHA® System **(van Wyk et al. *Vet Res* 2001, Kaplan et al *Vet Parasitol* 2004)**
    - Commonly used in sheep and goats to maintain refugia
    - Becoming the primary parasite control strategy
    - Treat animals based on pallor of ocular mucous membranes
      - Hematophagus *Haemonchus contortus*
    - Animals that are not anemic are left untreated as a source of refugia
    - Unfortunately not applicable to cattle



# Strategies to reduce resistance

- Targeted selective treatment (TST) to maintain refugia
  - Selecting which animals to treat
    - Treat a fixed % of the group
    - Treat based on some threshold (weight gain, FEC, pepsinogen)
    - Treat some classes or age groups but not others

https://www.beefmagazine.com/grazing-systems/ranching-101-rotational-grazing-offers-many-benefits

# Strategies to reduce resistance

- Adult beef cows as a source of refugia?
  - Well understood that cows develop immunity to nematode parasites with age
  - Possibilities
    - Leaving all adult cows untreated
    - Leaving oldest cows untreated
    - Leaving some % of cows untreated
  - Concerns
    - Impacts on production of cow and/or calf
    - Cow FEC's are generally low so impact on refugia?

https://beef2live.com/story-2016-cow-calf-production-shows-less-profitability-0-137147

# Strategies to reduce resistance

- Adult beef cows as a source of refugia?
  - Unaware of studies that explore this exact question
    - Studies with untreated control group also leave calves untreated
    - Other studies compare impacts of anthelmintics to each other

**The need for a source of refugia in beef cattle parasite populations is clear but information on the best way to achieve that goal is currently lacking**

# Strategies to reduce resistance

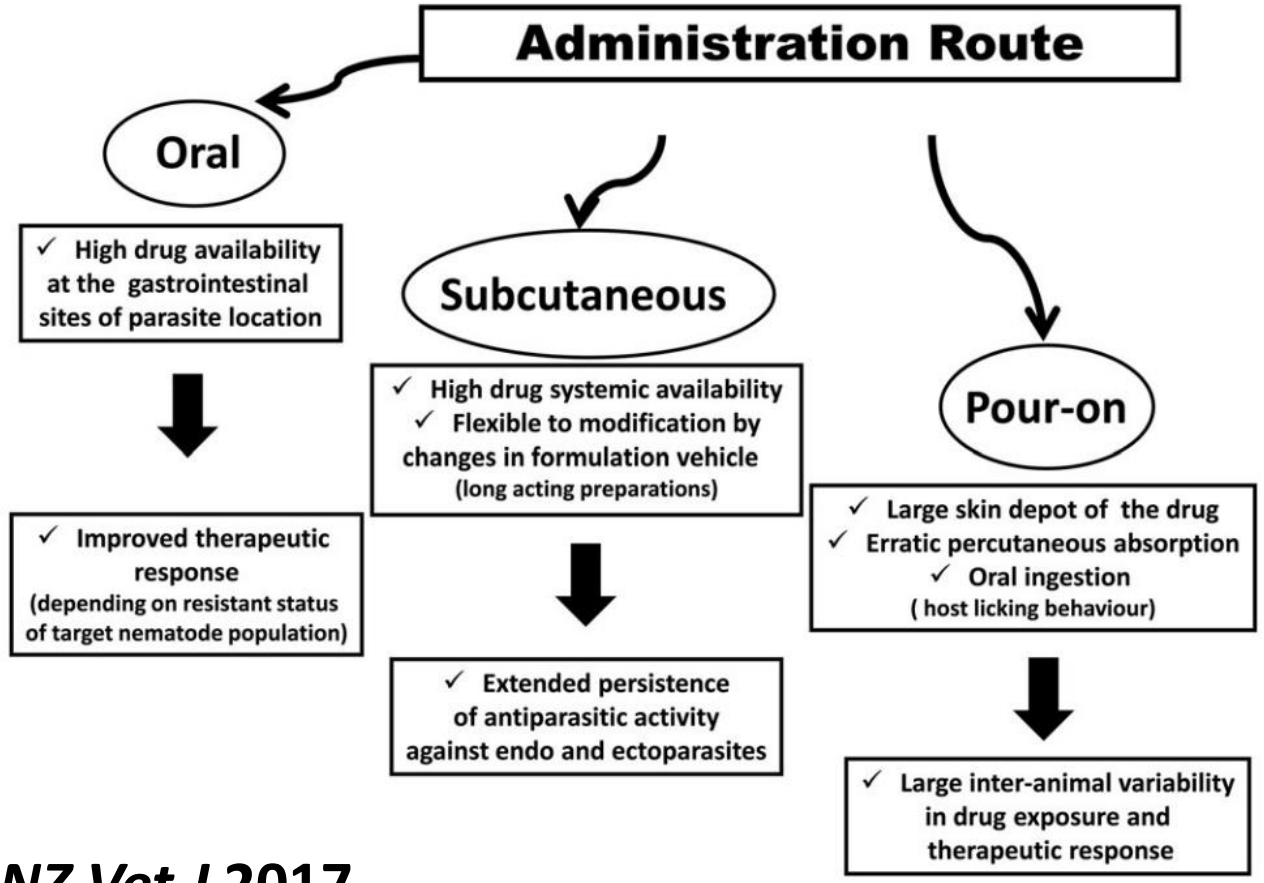
- Combination therapy
  - Administer 2 or more anthelmintics from different classes at the same time
  - Combination therapy typically more effective than either product alone

| Treatment | Day 0 | Day 14 | Day 32 | Day 61 | Day 88 | Day 117 |
|---|---|---|---|---|---|---|
| Saline | 36.0$^{ab}$ | 16.8$^{a}$ | 13.5$^{a}$ | 18.7$^{a}$ | 39.0$^{a}$ | 29.8$^{a}$ |
| Doramectin | 46.5$^{a}$ | 8.9 (47%)$^{ab}$ | 7.5 (44.2%)$^{a}$ | 14.9 (20.4%)$^{a}$ | 32.3 (17.2%)$^{a}$ | 37.3 (-25.0%)$^{a}$ |
| Doramectin + Albendazole | 42.8$^{a}$ | 0.2 (99.0%)$^{c}$ | 0.2 (98.8%)$^{c}$ | 7.9 (58%)$^{b}$ | 27.9 (28.3%)$^{a}$ | 26.3 (11.7%)$^{a}$ |
| Eprinomectin (ER) | 24.7$^{b}$ | 4.8 (71.3%)$^{b}$ | 3.9 (70.9%)$^{b}$ | 4.9 (73.6%)$^{b}$ | 8.6 (77.8%)$^{b}$ | 13.0 (56.4%)$^{b}$ |

**Edmonds et al. *Vet Parasitol* 2018**

# Strategies to reduce resistance

- **Route of administration**
  - Pharmacokinetics determine the drug dose reaching the target parasites
  - Route of administration impacts the pharmacokinetics




- Recent review by **Lifschitz et al. *NZ Vet J* 2017**

Lifschitz et al. *NZ Vet J* 2017

# Strategies to reduce resistance

- Route of administration
  - **Pour-on products tend to produce lower and more variable drug concentrations at the parasite level**
    - Leathwick et al. *Vet Parasitol* 2016
    - Gokbulut et al. Vet Parasitol 2010
    - Sutherland et al. *Trends in Parasitol* 2011
    - Gasbarre et al. *Vet Parasitol* 2014
  - Other concerns with pour-on formulations
    - Licking **(Laffont et al *Int J Parasitol 2001*, Bousquet-Melou et al. *Int J Parasitol* 2011)**
    - Weather **(Sargent et al *Vet Parasitol* 2009)**

# Moving forward…..

- Assess current anthelmintic program
  - If effective, stick with it
    - May find that some groups of cattle may not need to be dewormed
  - If not, investigate why
- Combination therapy may be needed
- Consider adopting strategy to increase refugia
- Use products according to label directions
  - Dose, application method etc
- Use products for intended purpose
  - Don’t use anthelmintic products to control other parasites

# What you learned today

- Apparent anthelmintic resistance appears to be widespread in OK cow-calf herds
- Composite sampling may be an effective way to detect anthelmintic resistance at the herd level

- **Anthelmintic programs currently employed by participating herds appear to be largely ineffective**
  - More work is needed to fully assess the prevalence and impact of anthelmintic resistance

# What you learned today

- We can no longer assume that traditional parasite control programs are effective
  - Resistance to all available classes of anthelmintics has been detected
  - Resistance has been identified from a variety of production systems and geographic locations
- Monitoring effectiveness of parasite control programs is becoming critical
- There is a need for science based refugia programs in cattle
- Our parasite control programs should be adapted to the current climate of increasing drug resistance

# Questions

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