Approval Date: October 5, 1998

# FREEDOM OF INFORMATION SUMMARY

## I. GENERAL INFORMATION

### A. File Number

NADA 041-061

### B. Sponsor

Pfizer, Inc.
812 Springdale Drive
Exton, Pennsylvania 19341-2803

### C. Proprietary Name

Mecadox® 10 Type A Medicated Article

### D. Established Name

Carbadox

### E. Dispensing Status

OTC

### F. Dosage Regimen

Mecadox® 10 is administered ad libitum in a final feed at a concentration of 10, 25, or 50 grams per ton.

### G. Route of Administration

Mecadox® 10 is administered orally in finished feed.

### H. Indication

Mecadox® 10 is indicated for the control of dysentery and bacterial enteritis and for growth promotion in swine.

### I. Effect of Supplement

Provides for the establishment of a 42 day slaughter withdrawal period for carbadox in swine tissues and a limitation against use in pregnant swine or swine intended for breeding purposes.

## II. EFFECTIVENESS

Studies demonstrating the efficacy of carbadox for the control of dysentery and bacterial enteritis and for growth promotion are documented in the Freedom of Information (FOI) Summary for the original approval for MecadoxÒ 10 under NADA 41-061.

## III. TARGET ANIMAL SAFETY

Studies demonstrating the safety of carbadox for use in swine is contained in the FOI Summary for the original approval for MecadoxÒ 10 under NADA 41-061.

## IV. HUMAN FOOD SAFETY

A. Toxicity Studies: As documented in the Freedom of Information (FOI) Summary for NADA 41-061 dated January 30, 1998.
B. Safe Concentrations of Total Residues: As documented in the FOI Summary for NADA 41-061 dated January 30, 1998.
C. Total Residue and Metabolism Studies: As documented in the FOI Summary for NADA 41-061 dated January 30, 1998.
D. Determination of the tolerance for the marker residue: As documented in the FOI Summary dated January 30, 1998, FDA selected liver as the target tissue and quinoxaline-2-carboxylic acid (QCA) as the marker residue. FDA determined that when QCA (marker residue) is at or below 30 ppb in the liver (target tissue) no residue of carcinogenic concern is detectable in each of the edible tissues by any method.
E. Determination of the Withdrawal Time: Study Number 2522A-60-97-077
    1. Purpose: A tissue residue study was conducted to determine the depletion profile of quinoxaline-2-carboxylic acid (QCA) residue in uncooked porcine liver and muscle tissue following oral administration (via the feed) of carbadox (Mecadoxâ 10) for 28 days at 55 ppm (50 grams per ton) to growing swine.

    2. Investigators: This study was conducted in two phases.
    Phase one (live phase):

    Martha Ferris, D.V.M., M.S.
    Colorado Animal Research Enterprises, Inc.
    Fort Collins, CO 80524

    Phase two (analytical phase):
    Dr. Joe Boison
    Government of Canada
    Canadian Food Inspection Agency
    Centre for Veterinary Drug Residues
    Saskatoon, SK

    3. Animals: Thirty-four crossbred pigs (17 gilts and 17 barrows)

    4. Dosage form: Feed containing 55 ppm carbadox.

    5. Pertinent parameters measured: Muscle and liver were collected from each animal for QCA residue analysis. All of the tissue samples were analyzed in triplicate. For the purpose of establishing a withdrawal period only the liver residues were used.

6. Results: See Table 1.

   Table 1: Arithmetic means (± SD) for quinoxaline-2-carboxylic acid (in ppb) in uncooked liver and muscle tissue of growing swine fed carbadox at 55 ppm for 28 days

| | | | QCA Concentration | |
|---|---|---|---|---|
| Treatment Number | Days Carbadox Withdrawn | No. of Animals | Liver | Muscle |
| T2 | 14 | 5 | 51.93+15.14 | <LOQ* |
| T3 | 21 | 5 | 29.09+8.20 | <LOQ |
| T4 | 28 | 5 | 7.72+4.72 | <LOQ |
| T5 | 35 | 5 | 11.23+1.86 | <LOQ |
| T6 | 42 | 3 | 11.16+2.13 | <LOQ |
| T7 | 49 | 1 | 10.90+2.35 | <LOQ |

   *LOQ liver, muscle = 5 ppb
   LOD liver, muscle = 2 ppb

7. Withdrawal period determination: A tolerance of 30 ppb was previously established for QCA (the marker residue) in swine liver (the target tissue). The withdrawal period was based on a statistical analysis of the depletion data, using an upper tolerance limit containing 99 percent of the population with a 95 percent confidence limit. Using the uncorrected residue data for liver from Days 14 to 49, a withdrawal period of 39.34 days was calculated. Based on this data, a 42-day withdrawal period was assigned for the use of MecadoxÒ 10 in swine.

F. Regulatory method: Residues of quinoxaline-2-carboxylic acid are determined using a gas chromatographic assay with electron capture detection. The method has a limit of quantification of 5 ppb. The method is on display in the Dockets Management Branch (HFA-305), Room 1061, 5630 Fishers Lane, Rockville, Maryland 20852.

## V. AGENCY CONCLUSIONS

A tolerance of 30 ppb was previously established for QCA (the marker residue) in swine liver (the target tissue). With this supplemental NADA, a pre-slaughter withdrawal period of 42 days was assigned for the use of MecadoxÒ 10 (carbadox) Type A Medicated Article in swine feed. The withdrawal period was based on a statistical analysis of the depletion data, using an upper tolerance limit containing 99 percent of the population with a 95 percent confidence limit. The Limitations section in 21 CFR 558.115 will be amended to reflect the 42-day withdrawal period.

In accordance with 21 CFR 514.106(b)(2)(x), this is a Category II supplement. The approval of this change required a reevaluation of the slaughter withdrawal period

according to current food safety guidance. Accordingly, this approval did not require a reevaluation of target animal safety or effectiveness data in the parent application.

The agency has determined under 21 CFR 25.33(a)(1) that this action is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Mecadox® 10 is not currently under any unexpired U.S. patents.

## VI. LABELING (ATTACHED)

1. Facsimile Bag Label - Mecadox ® 10 Type A Medicated Article
2. Specimen (Bluebird) Type B Feed Medicated Feed
3. Specimen (Bluebird) Type C Feed Medicated Feed

Copies of applicable labels may be obtained by writing to the:

Food and Drug Administration
Freedom of Information Staff (HFI-35)
5600 Fishers Lane
Rockville, MD 20857

Or requests may be sent via fax to: (301) 443-1726. If there are problems sending a fax, call (301) 443-2414.

The format of this FOI Summary document has been modified from its original form to conform with Section 508 of the Rehabilitation Act (29 U.S.C. 794d). The content of this document has not changed.