Interagency Response to Public Comments on the Risk Assessment for the Public Health Impact of Highly Pathogenic Avian Influenza Virus in Poultry, Shell Eggs, and Egg Products

Conducted by FSIS in collaboration with FDA and APHIS

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1 Executive Summary[10]

Introduction

In 2006, the National Chicken Council and the National Turkey Federation requested the USDA Food Safety and Inspection Service (FSIS) to conduct a risk assessment for Asian lineage highly pathogenic avian influenza virus (HPAIV) H5N1. An interagency workgroup was formed between the USDA Animal and Plant Health Inspection Service (APHIS) and the HHS Food and Drug Administration (FDA) and FSIS. Beginning in December, 2008, FSIS requested public comment on a draft quantitative food safety risk assessment for HPAIV H5N1 associated with the consumption of poultry products, shell eggs, and egg products (Docket No. FSIS 2007–0001). The purpose of this risk assessment was to: (1) estimate the public health impact from human exposure to an HPAIV index flock through the consumption of contaminated poultry products, shell eggs, and egg products, and (2) evaluate the relative effectiveness of strategies to reduce or prevent exposure to HPAIV from the consumption. The comment period closed March 4, 2009[11].

Input for the improvement of the risk assessment was requested in four general topic areas: the assumptions made, the modeling techniques used, the data used, and the clarity of the risk assessment document. Comment summaries and responses are grouped by topic. Original comments can be found at www.regulations.gov.

Revised Model Outputs

Poultry Model

- The revised poultry model predicts there is an approximate 95% and 98% chance that the HPAIV-infected chicken and turkey index flock, respectively, would be identified and prevented from entering slaughter. This is an increase over the previous model estimates of 94% and 98%, respectively.

- The revised poultry model predicts a 41% decrease in expected human illnesses, compared to the previous baseline, from the index infected chicken flock and turkey flock.

Egg Model

[10] This document is in support of the main report, Interagency Risk Assessment for the Public Health Impact of Highly Pathogenic Avian Influenza Virus in Poultry, Shell Eggs, and Egg Products, and should not be read outside of the context of that report.

[11] All comments officially received through regulations.gov and through the "For Further Information Contact," of the Federal Register Notice (December 2, 2008, Vol. 73, No. 232, Pg 73240-73242) by the March 4, 2009 official deadline were addressed by this report.

- The revised egg model predicts the HPAIV-infected index hen flock would result in 1,083 HPAIV-contaminated eggs before the flock is discovered as HPAIV-positive. This is a decrease from the original model estimate of 11,293 HPAIV-contaminated eggs.

- The revised egg model continues to predict zero illnesses.

- Removal of HPAIV-positive eggs from commerce was evaluated as a potential mitigation strategy to reduce exposure. The revised egg model predicts that 98% of contaminated eggs would be removed with a 2 day market withdrawal. This is an increase from the original model prediction of 97%.

Mitigations

- The revised poultry model contains two additional mitigations steps, use of morbidity and feed intake. Incorporation of visible morbidity resulted in a 95.5% chance an infected chicken flock would not be sent to slaughter. This is an increase over the revised baseline estimate of 94.7%. Expected human illnesses decreased by ~8-fold. Incorporation of feed intake resulted in a 96% chance an infected chicken flock would not be sent to slaughter and expected human illnesses decreased by ~22-fold.

Key Model Changes

Virus levels in meat: As recommended in the public comments, the poultry model was updated to include data from Das et al., 2008 to estimate the virus levels in the meat of infected birds. Virus titers from breast and thigh meat samples were used in the model in place of the original baseline values. This resulted in a 5-fold increase number of expected illnesses over the baseline predictions.

Daily mortality threshold: Commenters suggested that the daily mortality threshold trigger to not send a flock to slaughter was incorrect. For the poultry model, Vieira et al., 2009, was used to calculate a daily mortality threshold trigger of 0.17% for chicken and turkey flocks. For the egg model, a 0.5% hen daily mortality trigger was calculated from Iowa State University unpublished data. Compared to the original poultry and egg baseline, these changes resulted in ~4-fold reduction in expected human illnesses and a 58% reduction in HPAIV-contaminated eggs, respectively.

Percent of eggs contaminated: Following reviewer's suggestion, the fraction of contaminated eggs was reduced to 55% (Beard et al., 1984; Swayne and Suarez, 2007). The revised baseline model predicted a 75% decrease in the number of contaminated eggs from the original baseline predictions.

Summary

The Interagency workgroup made several changes to improve the poultry and egg models in response to comments received from the public. The revised poultry model predicts an increase

in the probability that an infected index flock would be discovered prior to slaughter. The revised model also predicts that in the unlikely event a flock went to slaughter, there would be fewer expected human illnesses. The revised egg model continues to predict zero human illnesses. Further, it predicts fewer contaminated eggs and a greater percentage of potentially contaminated eggs being successfully removed from the market following a recall. This risk assessment was developed as a tool requested by industry. The risk assessment does not attempt to estimate absolute numbers of illnesses or exposures, but rather to use such estimates as a means to explore mitigation strategies.

2 Assumptions

2.1 Predicted frequency of eggs produced and predicted frequency of egg contamination

COMMENT: Commenters suggested the two following issues should be reconsidered: 1) the frequency of egg produced by an HPAIV-infected flock (drop in egg production), and 2) the frequency of HPAIV-positive eggs produced by an HPAIV-infected flock.

RESPONSE: Though the Interagency workgroup agrees that a drop in egg production frequency is possible for a layer flock infected with Asian lineage H5N1 virus, no quantitative data were identified nor provided to model a drop in egg production. One commenter suggested that the Beard et al., 1984 egg drop data were ignored. Pages 88-90 of the original report quantify the affect these of data in the egg model (further, the Beard data are used elsewhere when appropriate). Even though both strains are HPAI, these data were not incorporated in the baseline model given that H5N2 virus, used in the Beard study, and the Asian lineage H5N1 virus, used in Das et al., 2008, appear to behave differently. For example, the first and last time points that infected H5N2 chickens were observed to die was 4 and >20 days (2 of 25 birds survived), compared with 1.5 and 1.75 days for H5N1 (19 of 19 dead). Though these observed differences might not be due to strain characteristics, it was reasonable not to incorporate these data into a baseline model for Asian lineage H5N1.

Comments regarding the frequency of HPAIV-positive eggs were appreciated and the following changes were made to the baseline model: "Egg Contamination Option 3" has replaced the previous baseline. This assumes that 55% of eggs laid after the first 19 hours are all contaminated. Beard et al., 1984 and Swayne et al., 2008 suggest 50-60% of the eggs laid would be contaminated if there were no drop in egg production.

The revised baseline model predicts a 75% decrease from the original baseline predictions to 2,827 HPAIV-positive eggs.

2.2 On-farm flock morbidity

COMMENT: Commenters were concerned that morbidity of HPAIV-infected birds was not adequately accounted for in the model and that the identification of sick birds would decrease the probability of an infected flock going to slaughter. In the original model, percent daily morbidity was not used to estimate the probability that a flock is not sent to slaughter; only percent daily mortality was used. Commenters suggested that this be added to the risk assessment.

RESPONSE: Morbidity has not been added to the baseline model for the following reasons: 1) clinical signs are generally not diagnostic for HPAI and might not present during an outbreak (Spickler et al., 2008), and 2) the Das et al., 2008 morbidity data are based on observations of "depression and dehydration". Such "low grade" morbidity would not likely be enough to prevent a flock that has reached market weight from being sent to slaughter.

Given that this risk assessment was developed as a tool to explore mitigations, the Interagency workgroup agreed that it might be helpful to explore the effect of using morbidity as an indicator. Therefore, morbidity has been incorporated into the model as an option. Users may now run the model choosing whether or not to factor in morbidity.

To incorporate the effect of morbidity in the model, two types of data were needed: 1) time course of morbidity, and 2) threshold of daily morbidity that would cause farms not to send a flock to slaughter. Das et al., 2008 were used to estimate the morbidity time course (see table below).

Time (Hour)	Morbidity		
	+	n	Input
0	0	10	0
6	0	10	0
12	0	10	0
18	0	10	0
24	9	10	0.9
30	10	10	1
36	6	10	1
42			1
48			1

Table. Pathogenesis of HPAIV at different post-inoculation time points in chickens intranasally inoculated with A/WhooperSwan/ Mongolia/244L/05 H5N1 (see main report, table 4).

No data were identified, however, to estimate the threshold of daily morbidity that would cause farms not to send a flock to slaughter. Therefore, it was assumed that the same threshold for mortality was sufficient for this scenario. Given that morbid and dead birds might be removed from production at the same point in time, the number of morbid birds estimated by the transmission model was added to the number of dead birds for each day. These values were used to estimate the percent of the flock that was presenting morbidity and had died for a given 24-hour period.

When percent daily morbidity was included, the probability of identifying an infected chicken flock prior to slaughter increased from 94% to 95%. The probability of identifying an infected turkey flock prior to slaughter remained at roughly 98%. The expected number of illnesses

decreased from 0.759 to 0.111 for the index chicken flock (20,000 birds) and from 2.37 to 0.374 for the index turkey flock (9,000 birds).

2.3 Feed and water intake

COMMENT: Commenters reported that feed and water intake is closely monitored among poultry flocks and that a drop in intake would alert a grower to possible disease. In the 2003 Low Pathogenicity Avian Influenza (LPAI) outbreak in Connecticut, a drop in feed and water consumption was observed before mortality. Commenters suggest this drop in feed and water intake should be included in the model as a factor affecting the early detection of an infected flock.

RESPONSE: The Interagency workgroup agrees that feed and/or water intake could provide a potential early detection for the index flock. However, there is no evidence to show that Asian lineage H5N1 HPAIV-infected birds manifest a significant drop in feed and/or water intake before mortality would reveal the flock as HPAIV-positive. The LPAI example[12] is not representative given birds with LPAI survive much longer than those infected with HPAIV.

To address the comment, the morbidity component that was added to the poultry model can be used (see section 2.2 On-farm flock morbidity). The first piece of information needed is a time course indicating the fraction of a commercial flock population that stops eating. These data were not available, so it was assumed that birds could quit feeding when clinical signs for HPAI are present (Das et al., 2008; see table above). These data were combined with the mortality output of the model given that dead birds would not consume feed. The second piece of information was the threshold at which poultry farm managers would detect a change. The revised daily mortality threshold was used (see section 2.5 Daily mortality flock threshold for chickens and turkeys). Incorporation of these data into the revised model gave the following results: the probability of a flock not being sent to slaughter increased to 95.5% from the revised baseline estimate of 94.7%; expected illnesses decreased by 8.4-fold.

Given that this risk assessment was developed as tool to investigate mitigations, users can change the above assumption. For example, if a user determines that evidence of viral systemic infection is more appropriate, data from Das et al., 2008 on the presence of virus in heart, breast and thigh muscle could be used (see table below). Incorporation of these data into the revised model gave the following: the probability of a flock not being sent to slaughter increased to 96% from the revised estimate of 94.7%; expected illnesses decreased by ~22.55-fold.

	Average of Trachea, Heart, Breast, and Thigh recovery by either method		
Time (hrs)	**+**	**n**	**Input**

[12] FSIS followed up with the commenters on the 2003 Connecticut outbreak. A grower generously provided chicken feed consumption weekly data from 33 flocks during a single month (33 points). The average weekly feed intake was 23.3 lbs/100 birds, s. d. 2.3 (ranged from 19.9 to 28.5) over 6 species of birds. Additional data were requested to represent seasonal variation. Given the need for a data set that would be representative of the entire chicken, turkey, and layer industry, these data were not incorporated into the revised risk assessment.

0	0	80	0
6	12	80	0.15
12	13	80	0.1625
18	41	80	0.5125
24	73	80	0.9125
30	78	80	0.975
36	80	80	1
42	152	152	1
48	44	44	1

Table. Detection of HPAIV at different post-inoculation time points in chickens intranasally inoculated with A/WhooperSwan/ Mongolia/244L/05 H5N1 (see main report, table 4).

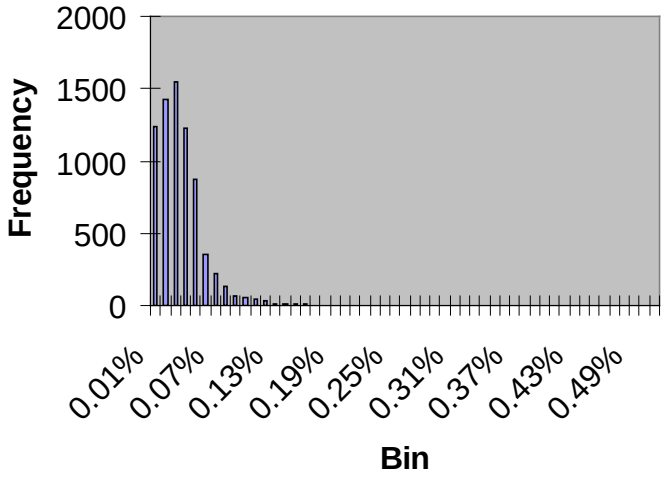
2.4 Daily mortality hen flock threshold

COMMENT: Commenters suggested changing the baseline detection threshold for layers to reflect current industry practices. The original baseline assumed that detection of the index flock will occur when 2% daily mortality is reached. Commenters suggested that the model should assume that the baseline threshold for disease detection occurs when either 1) 0.5% mortality is detected on any one day; or 2) 0.25% mortality is exceeded on 2 consecutive days.

RESPONSE: A revised estimate of the baseline detection threshold for table-egg layer flocks using normal mortality data was developed. Normal daily mortality in table-egg layers is experienced throughout the production cycle. In the event of a HPAI outbreak, the total daily mortality pool will contain birds that die as a result of HPAI disease as well as birds that die from other causes. In order to estimate the number of birds that die from other causes, daily data from commercial table-egg layer flocks were requested for analysis.

Since daily mortality data records are not commonly kept, these data were provided by the egg industry through Iowa State University by special request. Data from 12 flocks, 4 flocks each from the 3 major egg layer breeds in the U.S., represent one entire production cycle (84 weeks on average). These data are less representative of the variation between layer operations across different geographic regions as compared to the data provided by AgriStats Inc.

Daily mortality data: There were 7113 data points in this data set. The mean daily mortality was 0.031% (s.d. 0.027%). A histogram of the daily mortality data is provided in the figure below.



Given a data set with 7113 data points, these data (empirical distribution) were directly used for conducting the analysis. Based on the daily data, the probability that the daily mortality is less than 0.25% is 99.9%. The probability that the daily mortality is less than 0.5% is 99.97%.

Given the analysis, a 0.5% is a conservative limit for normal daily mortality for a table-egg flock. Because normal daily mortality rarely exceeds 0.5% each day, this threshold may be used as an upper bound for an extreme event in the baseline model scenario. The analysis of daily mortality also shows that the probability of daily mortality being more than 0.25% is less than 0.1% each day. There were no instances when the mortality was higher than 0.25 for two consecutive days. Although using a detection threshold of 0.25% on two consecutive days could be more specific for HPAIV detection, additional time is required for detection to occur compared with a threshold of 0.5% on one day. The extra time taken for discovery of infection would result in an increase in the release of contamination.

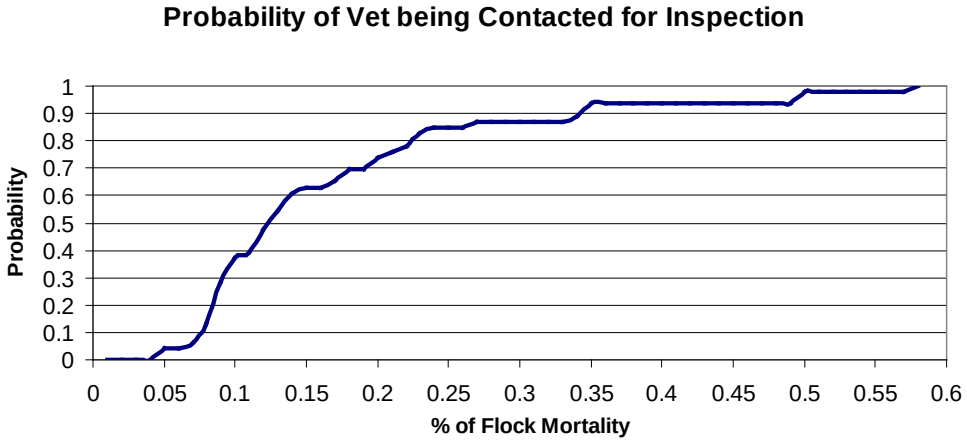
The revised baseline model predicts a 58% reduction (4,779 contaminated eggs) from the draft baseline model. A recall of those eggs produced within the last 2 days would remove roughly 98% of the contaminated eggs from commerce. A recall of the last 3 days of eggs would remove 99.7% of contaminated eggs.

2.5 Daily mortality flock threshold for chickens and turkeys

COMMENT: Similar to the comments on daily mortality thresholds among hen flocks, commenters recommended a lower daily mortality threshold for detecting an HPAI outbreak within a broiler flock. The 0.5-2% daily mortality was considered conservative, and values of 0.1% for chickens and 0.2% for turkeys were suggested.

RESPONSE: The daily mortality threshold for both chickens and turkeys has been revised in response to public comments. A study by Vieira et al., 2009 surveyed growers as to the level of daily flock mortality that would cause them to contact a veterinarian. For broilers greater than 28 days old, growers reported what percent daily mortality would cause them to contact a

veterinarian. The average percent daily flock mortality that would trigger a call to a veterinarian was 0.17%. Unpublished raw survey data on daily mortality for broilers was obtained (Vieira, personal communication). A cumulative distribution of these values was used in the model to estimate the percent daily mortality that would trigger a call to a veterinarian and thus the identification of an HPAIV-infected flock. This is shown in the figure below. Under mortality model options for mortality at the farm, option 2 now uses this survey data.



Using the survey data from the Vieira et al., 2009, the revised baseline model predicts for chickens 0.162 expected human illnesses, as compared to 0.759 expected human illnesses. For turkeys, there were 0.535 expected human illnesses, as compared to 2.37 expected human illnesses.

2.6 Egg removal due to inspection

COMMENT: A comment indicated it was unclear why a baseline of 5% infected eggs failing inspection was chosen given studies showing that 10-30% of infected eggs were abnormal or thin shelled. The commenter states, "We would submit that rejection of these types of eggs will be very high because of breakage and packaging failure issues associated with automatic and assisted packing systems used in egg operations holding 100,000 hens or larger flocks. In addition, egg rejection at far less than 5% would also be a big signal that something major was wrong with the flock."

RESPONSE: To address the reviewer's comment, the baseline value for egg removal was increased to 10%. Though the commenters did not provide citations to specific references to support their assertion, Cappucci et al., 1985 suggests that 10% of H5N2 HPAIV-contaminated eggs from a commercial flock would be misshapen, small, or soft-shelled. Additional H5N2 data were identified that showed at 48 hours, 12.5% (2/16) of eggs from experimentally infected chickens were thin/soft shelled (J. Beck, personal communication). Given that the Cappucci et al., 1985 data were from a commercial flock, these data were used.

Regarding the final comment that an egg rejection rate of "far less than 5%" would be a signal to a problem, there are two confounders that would make detection difficult: 1) As the transmission model shows, different numbers of contaminated eggs are produced over a series of days.

Therefore, not all infected eggs would be processed at one moment in time, and 2) the 5% value was 5% of HPAIV-contaminated eggs and not for all eggs produced by the infected flock (or even eggs that may be processed from other flocks). Therefore, there would be a dilution effect.

Commenters do not provide a level at which egg rejection would trigger a hold on egg movement, making it difficult to incorporate into the model. Importantly, increasing or decreasing the number of eggs removed due to inspection does not impact the previous results of the risk assessment, that is, no human illnesses are predicted and a recall of at least 2 days of egg production, once the flock is identified as HPAIV-infected, would be needed.

2.7 Dose-response model

COMMENT: Commenters expressed that the dose-response model was not appropriate because it was based upon human intranasal studies, not oral ingestion of HPAIV.

RESPONSE: The Interagency workgroup appreciates the comment regarding the dose-response model used in the risk assessment. The dose-response model developed using human intranasal studies is likely different from what the dose-response relationship would be for oral ingestion and that a dose-response model based on human oral ingestion of HPAIV would be more appropriate. At this time, however, we have been unable to identify any new sources of data to develop a dose-response model specifically for human oral ingestion of HPAIV. Furthermore, no such data has been provided by the commenters.

2.8 Latency

COMMENT: One commenter states "Detection of viral RNA in tissues is not synonymous with release of infectious virus from a natural orifice. Antigen (an accepted surrogate for infectious virus) was first detected in the trachea at 18 hours post infection. In the absence of data that infected birds are contagious before virus is detected from a natural orifice, it is not reasonable to assume they can spread the disease to others just because virus is detected in muscle."

RESPONSE: The Interagency workgroup agrees that the data used represent a surrogate. The reviewer is suggesting that we use the Das et al., 2008 data generated by antigen testing vs. RNA testing. The Interagency workgroup respectfully disagrees that antigen testing is superior in this case. Positive antigen or nucleic acid tests do not guarantee the presence of infectious virus. Unfortunately, the reviewer does not provide support for their statement. Further, only 15 to 16% of latent birds at 6 and 12 hours respectively are estimated to be able to spread the virus. The baseline for latency remains the same. Model users are welcome to make changes to the baseline that fit their understanding and situation. For this purpose, the Das et al., 2008 trachea by antigen detection has been added as model option 24 (see table below).

Option	Trachea by antigen testing

24			
Time	**+**	**n**	**Input**
0	0	10	0
6	0	10	0
12	0	10	0
18	1	10	0.1
24	6	10	0.6
30	8	10	0.8
36	10	10	1
42	19	19	1
48	11	11	1

Table. Detection of HPAIV at different post-inoculation time points in chickens intranasally inoculated with A/WhooperSwan/ Mongolia/244L/05 H5N1 (see main report, table 4).

3 The modeling techniques

COMMENT: "It's unclear how human illnesses associated with the consumption of HPAI containing eggs are calculated for the egg model and the results are not summarized. For example, section 6.3.3.4 (pg 103) shows that 9.5 illnesses are expected at time 0 days to reach market shelf. Given the various parameters used, this particular illness calculation is seemly based on 11,293 infected eggs, a consumption rate of one egg per consumer at a 4.9 Log_{10} EID_{50} per ml level, and a conservative intranasal dose response estimate between 7.8 to 9.5 Log_{10} EID_{50} (just below Table 18, pg 74). It would seem that one raw egg per consumer, even if they put it in their nose, would not meet the minimum infectious dose. And 10 or 100 raw eggs per consumer could not be assumed to contain AI virus if flock/farm prevalence is <10%. Egg prevalence of 10% would occasionally result in 2 eggs per carton being infected, and rarely as many as three. We would ask that more information be shown (perhaps a table summary) to better demonstrate the model outcome for eggs."

RESPONSE: The commenter's confusion stems from a misunderstanding of ID_{50}. The dose-response indicates an ID_{50} of ~8.7 log_{10} EID_{50}. This means that the amount of virus, measured in EID_{50}, needed to observe a 50% probability of illness, is 8.7 log_{10} EID_{50}. This is not the *minimum* infectious dose as indicated by the reviewer. Illnesses can occur at lower virus levels; however, the probability of such an occurrence is lower (*i.e.,* a consumer does not need to put an egg in their nose for there to be a sufficient virus level for some probability of illness.) Further confusion appears to stem from the metric for the virus level in the egg (log_{10} EID_{50} *per mL*). The original model assumed a 60 mL egg, so the final exposure level, if one consumed a single infected egg, would be 6.7 log_{10} EID_{50} (79,433*60). At this level of exposure, the model predicts there is approximately a 0.67% chance of becoming ill. Finally, it should be noted that the 11,293 contaminated eggs is the value before inspection. Assuming a 5% inspection removal rate, 10,728 contaminated eggs could be expected to enter commerce. Finally, the section referred to by the commenter does not reflect the baseline model. No human exposure or illnesses are predicted by the egg model.

4 Data used

4.1 Consumer cooking temperatures

COMMENT: Commenters suggested that the data used to represent the cooking practices of consumers (1999 U.S. Food Temperature Evaluation Home Cooking Temperature Summary) might be outdated. Use of recent data, if available, was encouraged.

RESPONSE: The HPAI poultry model used Audits International, 1999 U.S. Food Temperature Evaluation Home Cooking Temperature Summary to estimate the temperatures at which consumers cook poultry and eggs. Data were assumed to represent the peak temperature achieved by consumer cooking of chicken and turkey. In response to the comments, a new data set, EcoSure, 2007, has replaced the previous data set.

The EcoSure, 2007 survey provides updated data from the 1999 Audits International survey (figure below).

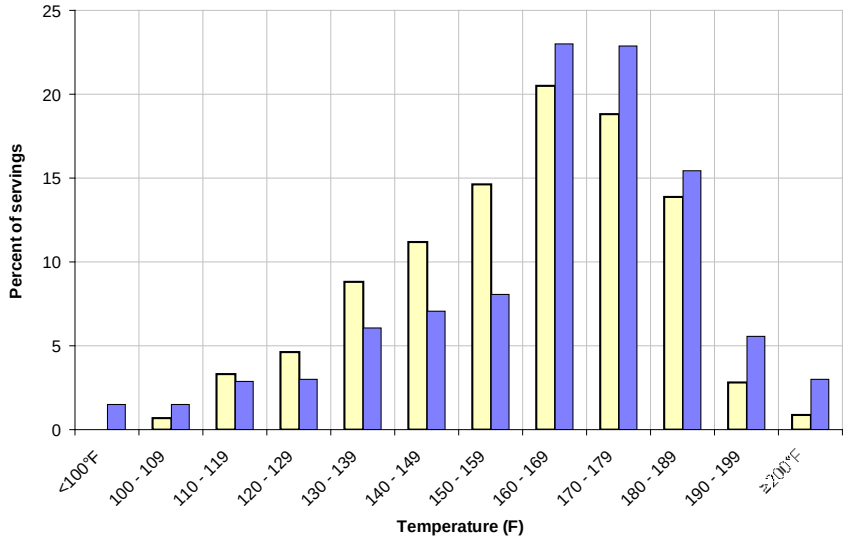


Figure. Comparison of EcoSure, 2007 (in blue) and Audits International, 1999 data.

Grouping the temperature data into four ranges, the percentage of servings cooked at various temperatures changes. This information is summarized in the table below.

Percent of chicken and turkey servings cooking at different temperature.

CATEGORY	TEMPERATURE RANGE (°F)	% OF COOKED POULTRY (AI, 1999)	% OF COOKED POULTRY (ECOSURE, 2007)
1	<100-139	17.4	15.0
2	140-149	11.2	7.1
3	150-159	14.6	8.1

4	160-≥200	56.9	69.9

To address the comments, the EcoSure, 2007 data have been incorporated into the poultry baseline model as Option 2 for cooking temperature. The expected number of human illnesses from chicken consumption is predicted to decrease from 0.759 (AI, 1999 data) to 0.634 (EcoSure, 2007).

4.2 Virus levels in eggs

COMMENT: The commenters suggested that different virus levels be used for egg yolk versus albumen in the model because the limited data available indicate that virus titers in albumen are 100 times greater than those found in the yolk. The differentiation between human exposure from yolk and albumen, was recommended.

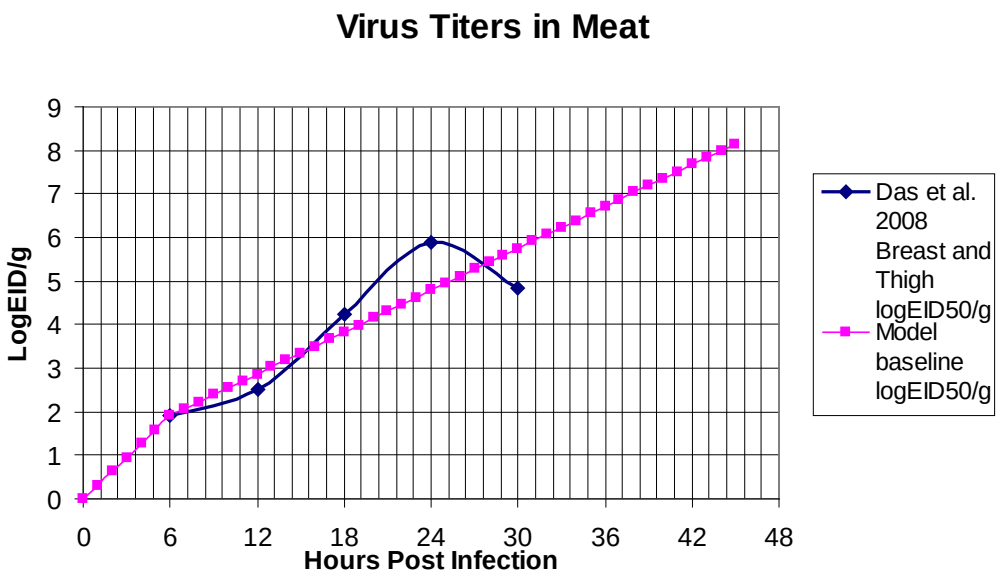
RESPONSE: While the Interagency workgroup agrees that virus titers differ for the yolk and albumen, with the latter having higher levels, the workgroup believes there is insufficient data to incorporate different levels in the model. To the workgroup's knowledge, H5N1 egg contamination data are not available; therefore, H5N2 data were used. The commenter suggests using Bean et al., 1985 who reported separate H5N2 virus levels for the yolk and albumen, with an approximate 100-fold difference between the two egg components. However, this difference is based on data from only three eggs. Additional H5N2 data were identified that also showed a difference between yolk and albumen levels, but this difference was approximately 10-fold (http://www.fao.org/docs/eims/upload//250703/aj162e00.pdf). It is important to note the model does not predict egg related human illnesses; therefore, lowering the infective levels in eggs to those levels reported for the yolk would not affect model outputs.

4.3 Virus levels in meat

4.3.1 Virus Levels in Meat at Various Time Points

COMMENT: It was suggested that data on virus levels in meat from Das et al., 2008 would more accurately estimate the virus level per gram of meat from HPAIV-infected birds at various time points post infection.

RESPONSE: The draft baseline model used three EID_{50} levels at three different time points: zero $\log_{10}$ EID_{50}/g at zero hours post-infection, 1.9 $\log_{10}$ EID_{50}/g (the minimum detection level) at 6 hours, and 7.7 $\log_{10}$ EID_{50}/g at 42 hours. The Das et al., 2008 data provide average meat virus titers across three tissue types: heart, thigh, and breast. The Interagency workgroup chose to use the average virus titers from thigh and breast meat only, as these are the tissues most commonly consumed. The data are provided at five time points: 6, 12, 18, 24, and 30 hours with corresponding virus titers of 1.9, 2.5, 4.25, 5.88, and 4.85 $\log_{10}$ EID_{50}/g. These values are shown in the figure below.



The model was run using the average breast and thigh levels (Das et al., 2008). Values for later time points were assumed to be 4.85 $\log_{10}$ EID_{50}/g[13]. The expected number of illnesses increased from the baseline of 0.759 to 3.79.

A number of inter-related factors contribute to the increase in illnesses observed using the new data including the tissue virus level at a given time point, percent virus allowed in muscle at a given time point, and mortality. At the earlier time points of infection (0-12 hours), there is relatively little virus available (2 to 3 $\log_{10}$ EID_{50}/g) and only 15 to 16% of infected birds are predicted to have virus within muscle, thus fewer possible infected servings. At the later time points (36 hours and greater), mortality rapidly increase and these dead birds do not contribute to contaminated servings. An increase in the virus levels can be expected to have the greatest impact between 12 and 36 hours. Therefore, the approximate 10-fold increase in EID_{50}/g at 24 hours from the original baseline resulted in the increased number of expected illnesses.

Based on the public comments, the Das et al., 2008 data now have been used to refine the model inputs for virus levels in meat at various time points in the revised version of the model. This provides a better estimate of the virus level per gram of meat as compared to the baseline values originally used, particularly at the 24 hour time point.

4.3.2 The Effect of Exsanguination on Virus Levels in Meat

COMMENT: It was suggested by one commenter that exsanguinated birds (*i.e.,* poultry slaughtered for consumption) would have lower levels of virus in their tissues than unexsanguinated birds (*i.e.,* the birds that were evaluated in the Das et al., 2008 study), and that this should be taken into account in the model.

[13] The 30 hr time point level was used for later points of infection. Das et al., 2008 stated "The virus titers did not appreciably change between 24 and 30 hr PI, indicating near saturation of virus replication after 24 hr PI."

RESPONSE: No comprehensive data sets that distinguish between virus levels in meat from birds that have been exsanguinated compared to those that have not, particularly for Asian lineage H5N1 HPAIV at various time points, have been identified. Further, the data cited by the commenter, as noted, is based on a non-Asian lineage HPAIV, making it difficult to compare. Although the data from Das et al., 2008 are from birds which were not exsanguinated and poultry slaughtered for human consumption in the U.S. are exsanguinated, these data remain the best available for modeling. Therefore, an effect of exsanguination has not been built into the model.

4.4 Serving size

COMMENT: A comment suggested "a 60 gram egg consists of about 6.6 grams of shell that is usually not consumed."

RESPONSE: The comment is appreciated and a change has been made in the model. The American Egg Board states shell weight is 9-12% of total egg weight. Assuming a 60 mL egg, edible content was estimated to be 53.7 mL.

4.5 Normal flock mortality

COMMENT: Two comments suggested that 0.3% daily mortality was incorrect for a broiler flock.

RESPONSE: The Interagency workgroup appreciates the comments and have changed the input. Unfortunately, no data were provided by the commenter. We have changed the daily mortality for a normal flock to 0.031%. See section 2.4 above.

5 Clarity of the document

COMMENT: A commenter suggested to run the egg model to estimate the human health impact of cooking to 145 ^{o}F given the FDA's food code requires cooking to 150 ^{o}F.

RESPONSE: The comment is appreciated. FDA's food code, depending on the method of cooking, suggests 145 ^{o}F for 15 seconds. Given a worst case scenario of contaminated eggs reaching market within 24 hours of lay, the model predicted 0.003 expected human illnesses.

COMMENT: Several commenters mentioned that the draft risk assessment should specify that the focus was Asian lineage H5N1 HPAIV.

RESPONSE: This comment is appropriate and the report has been updated.

COMMENT: One commenter said that the risk of an infected chicken flock going to slaughter, 6%, was "high" and therefore "conservative".

RESPONSE: The 6% figure comes from the non-detection window of 3.5 day (predicted by the transmission model). The data used to inform the transmission model are from young chicken intranasally infected with 5 $\log_{10}$ EID_{50} HPAIV. This is likely a substantial dose, in particular, as all birds experimentally received that same dose. Also, this dose was introduced via a sensitive route (compared with ingesting, which appears to be less sensitive (Swayne and Beck, 2005)). It is reasonable to assume that the larger the dose, the faster individuals birds would succumb to HPAIV. Given this, the draft results should not be conservative. This is evidenced by several HPAIV transmission model results suggesting a longer non-detection window where the virus spreads with little mortality (Spickler et al., 2008).

COMMENT: One commenter noted that emphasis on the probability a flock will or will not go to slaughter does not take into account the "entire story", for example the probability that a flock will become infected in the first place.

RESPONSE: This was outside of the scope of this risk assessment. APHIS is in the process of developing a risk assessment model to investigate the probability of Asian lineage HPAIV entering the US[14]. Further, this risk assessment was not developed to assess the total risk, but only that from the index flock and via consumption. The commenters suggest that incorporation of the probability HPAIV will enter the U.S. will lower the risk. However, the commenters failed to suggest that inter-flock transmission be incorporated. Certainly, more than one flock can become infected leading to an HPAI outbreak. This was evidenced in at least one well studied HPAI outbreak where approximately 250 commercial broiler, layer, and turkey flocks became infected (Stegman et al., 2004). Incorporation of inter-flock transmission would increase the human health risk. In addition, the risk assessment did not address occupational exposure or other routes of human exposure. This also would increase the human health risk. Commenters also note that HPAIV likely would be detected in migratory birds and live bird markets prior to commercial facilities. The Interagency workgroup agrees and suggests that this would heighten the already continued influenza surveillance making it less likely for human exposure through consumption. However, during the H7N7 HPAI outbreak in 2003, no previous signs were detected prior to commercial flock infection.

COMMENT: Commenters indicate the importance of cooking and consumer education.

RESPONSE: The Interagency workgroup agrees and appreciates the comment. However, it must mentioned that two nationally representative U.S. consumer surveys, Audits International, 1999 and EcoSure, 2007, demonstrate that 17.4 and 15.0% of consumers, respectively, cook their poultry to less than or equal to 139 ^{o}F. As the risk assessment demonstrates, mitigations at the farm are more effective compared with mitigation at the consumer level.

[14] http://www.aphis.usda.gov/vs/nahss/poultry/ai/avian_influenza_surveillance_plan_062907.pdf

6 Miscellaneous

6.1 Research Needs

COMMENT: It was suggested that more research be conducted on the following areas: 1) how standard industry practices, such as chlorine rinses, would affect virus levels, 2) morbidity, 3) HPAIV transmission as a function of season, temperature, humidity, ventilation, feeding system, watering system, bird density, cage design and cage density are a few factors, 4) HPAIV level in different cuts of meat and egg yolk vs. albumen, and 5) impact of exsanguination on virus levels in meat.

RESPONSE: The Interagency workgroup agrees with the suggested research needs. In particular, research elucidating industry practices or processing techniques that may potentially impact the level of virus found in or on poultry products including meat and eggs. If, and when, such data become available, this information could be incorporated into the model.

6.2 Improving Practices

COMMENT: A reviewer noted that during elevated infection risk, the risk assessment supports that use of flock testing to reduce the risk of sending an infected, yet undetected, flock to slaughter. The comment mentions that these "practices has been used by the industry on a pilot basis and during times of enhanced surveillance during LPAI incidents. Such procedures could be instituted during times of increased HPAI threat."

RESPONSE: The Interagency workgroup agrees and appreciates the comment. The risk assessment demonstrates the effectiveness of testing birds prior to movement from the farm to slaughter; however, it should be noted that the model predicts that testing is most effective when performed when the flock is ready to be sent to slaughter.

COMMENT: One commenter suggested that the baseline contact rate of 8 new infections per 6 hours per infected bird might not be appropriate given potential differences with European practices commercial poultry vs. U.S. practices.

RESPONSE: The commenter did not provide additional data and as such, a change was not made to the model. Further, this risk assessment was developed as tool to assess mitigation strategies and the impact of different contact rates can be explored.

COMMENT: Comments suggest that meat-types birds are not increasing in mass during the simulated grow-out period.

RESPONSE: The model accounts for different mass of birds at the point of slaughter. See section 4.4.3.3 of the main report and "Weeks in house" spreadsheet within the poultry model.

6.3 Theory/Overall Implications of the Risk Assessment

COMMENT: Commenters questioned the ability of HPAIV to cause human illness via consumption.

RESPONSE: There are two known cases of HPAIV human infection epidemiologically linked to consumption of duck blood (EFSA, 2006). This, the workgroup would suggest, is evidence. Further, this does not account for human cases not identified by surveillance, known human cases where the etiology is unknown, nor does it account for known human cases where consumption was the most likely source. At the 2008 Food Agricultural Organization - - World Health Organization (FAO-OIE-WHO) Joint Technical Consultation on Avian Influenza, it was noted that 4% of the 262 confirmed HPAIV human cases were attributed to "eating raw/poorly cooked poultry" (http://www.fao.org/docs/eims/upload//250682/aj158e00.pdf). This preliminary report has been mentioned in the revised risk assessment. Also, recent data suggest that consumption of HPAIV-contaminated chicken meat by pigs, ferrets, and mice cause infection and sometimes illness and death (Liptov et al., 2008; 2009).

One commenter cited Purchase, 1931 to suggest why duck blood could be more infectious than muscle to humans via ingestion. The commenter writes "Blood from HPAI-infected birds was shown in 1931 to be ten times more infectious than meat when given to chickens." The commenter concludes the 10-fold difference given that "Purchase reported that 0.5 ml of blood from a HPAI-infected chicken was infectious by the oral route for susceptible chickens, but it took 5 grams of meat to do the same." Unfortunately, the study did not actually measure virus within any tissues or blood. Further, the study does not reference the type of virus, only referring to it as "the virus of fowl-plague". It is not even clear if this is a single virus or cocktail. Though the study is worthy on its own merits, and we appreciate it being brought to our attention, comparing it to Asian lineage H5N1 HPAIV is not appropriate.

COMMENT: One commenter said that it was "difficult to envision, based upon current monitoring and surveillance systems, how the consumer could even be exposed to HPAIV. To estimate (imagine) the potential level of said virus that could be present in meat or eggs if such systems hypothetically failed to identify all infected birds challenges the current limits of science and reason."

RESPONSE: The Interagency workgroup agrees that the risk is low for the index flock; however, if the commenter has difficulty imagining a possible path to exposure, we would refer them to the following scientific publications and presentations: human exposure through duck blood (EFSA, 2006); FAO-OIE-WHO Joint Technical Consultation on Avian Influenza, where it was noted that 4% of the 262 confirmed HPAIV human cases were attributed to "eating raw/poorly cooked poultry" (http://www.fao.org/docs/eims/upload//250682/aj158e00.pdf); HPAIV-contaminated frozen duck meat entering commerce (Harder et al., 2009).

Furthermore, this risk assessment was developed as a tool requested by industry. It does not attempt to estimate absolute numbers of illnesses or exposures, but rather to use such estimates as a means to explore mitigation strategies.

COMMENT: One commenter noted, "There is a problem with assuming rinse fluid is equivalent to purge fluid. There is also a problem using the virus level from LPAI when a virus level for HPAI is present. This is another example of selective use of data."

RESPONSE: No additional data were provided; however, to address the second comment, the H5N2 HPAIV data now are employed. It should be noted that consumer cross-contamination, where these data are used, is not part of the baseline model, a non-conservative assumption that the commenter failed to mention.