From: Alsobrook, Lisa P.
To: Gaynor, Paulette M
Cc: Drozen, Melvin S.
Subject: FW: FSIS questions for the notifier concerning GRN 000927
Date: Thursday, August 6, 2020 9:04:00 AM
Attachments: image001.png
image002.png
image003.png
image004.png
image005.png
image006.png

Dear Dr. Gaynor,

This message responds on behalf of our client, Adept Limited, to the list of questions posed by the United States Department of Agriculture's (USDA) Food Safety Inspection Service (FSIS) regarding the Generally Recognized as Safe (GRAS) notice that we submitted to the Food and Drug Administration (FDA) for the intended use of polyvinyl alcohol (PVOH) as the primary component in water-soluble plugs for use in abattoirs to plug the anus of slaughtered sheep, lambs, and hogs. As you know, FDA filed the GRAS notice, designated as GRN 000927 on June 15, 2020.

FSIS's questions are marked by bullets in your July 16, 2020 email below, and are followed by our added responses in red. We hope and trust that the information below responds fully to FSIS's questions regarding Adept's GRN 000927. We look forward to FDA and FSIS's continued review of the Notice and we would be happy to provide you with any further information you may need.

Best regards,

Mel Drozen and Lisa Alsobrook
Melvin S. Drozen
Partner
Keller and Heckman LLP
tel: +1 202.434.4222 | fax: +1 202.434.4646 | drozen@khlaw.com
1001 G Street NW, Suite 500 West | Washington, DC 20001
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Associate
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From: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Sent: Thursday, July 16, 2020 9:05 AM
To: Drozen, Melvin S. <Drozen@khlaw.com>
Subject: FSIS questions for the notifier concerning GRN 000927

Dear Mr. Drozen,

FSIS has the following questions for the notifier concerning GRN 000927:

- What color is the plug and will it affect disposition of the viscera?

or pathological lesions in/on the viscera?

RESPONSE: The plug color is white. Given the speed of the slaughter process (500 or more hogs per hour), the plug would not be expected to have dissolved at the time the viscera are presented for inspection and would be visible to inspectors. Further, the plug is not expected to affect disposition of the viscera because the plug will not contact parts that are examined for contamination or pathological inspection of the viscera. The examples for swine viscera inspection, in the FSIS document, Animal Disposition/Food Safety: Post-mortem Inspection, 3/03/19, Entry Training for Public Health Veterinarian (PHV), do not include steps for any part of the viscera that would contact Adept's water-soluble plugs. Specifically, the PHV Entry Training document states:

> Viscera include the contents (organs) of the animal's abdominal cavity. You must be able to determine at all times which parts belong to a carcass. Therefore, the establishment must have a method of identifying the carcass and all its parts (e.g., tag). Viscera inspection includes the following steps:
> 1. Observe the eviscerated carcass, viscera, and parietal l (top) surface of spleen.
> 2. Observe and palpate mesenteric lymph nodes.
> 3. Palpate portal lymph nodes.
> 4. Observe dorsal (curved) surface of lungs.
> 5. Palpate bronchial lymph nodes – right and left.
> 6. Observe mediastinal lymph nodes.
> 7. Turn lungs over and observe ventral (flat) surfaces.
> 8. Observe heart.
> 9. Observe dorsal (curved) surface of liver.
> 10. Turn the liver over and observe ventral (flat) surface.

See page 12.

Further, the color of the plugs (white) would not be confused with contaminants such as feces or ingesta. The USDA FSIS Slaughter Food Safety Standard, 3-24-2020, Attachment , Identification of Contaminants for Livestock, A. Livestock Feces and Ingesta instructs the identification of feces and ingesta for swine and sheep/goats by color as "yellow, tan, brown, or green" and "green, brown to black," respectively. See page 21.

Additionally, no special inspection instructions are needed because any *de minimis* amount of plug material that could possibly remain on the finished product after washing (none is expected) would not present safety concerns and would not impact the organoleptic properties of the meat. (The dietary exposure evaluation of PVOH conservatively assumes that some PVOH could remain, although in practice, the PVOH will be completely removed).

- Is there a recommending washing procedure for the viscera to ensure complete removal of the plug?

RESPONSE: Adept does not recommend any special washing procedures because no special procedures are necessary. The rectal cavity is always flushed to remove the fecal matter and the

plug is washed out at the same time. Any cleaning procedures that are adequate for removing fecal contents, as required to produce human food, are reasonably expected to be more than adequate for completely removing the water-soluble plug. As reflected in FSIS Directive 9002, 7/30/10, Inspection and Export Certification of Livestock Intestines or Casings, for example, the intestines or casings must be visibly free of digestive tract contents to be considered clean.

- How much time /water does it take to dissolve the plug following the normal washing procedure?

RESPONSE: Under normal operating conditions, the plug does not dissolve during the quick washing process and is always flushed out. The plug dissolves when it is washed away with the fecal waste. The time required to dissolve the plug, after it is removed, will depend upon the volume, flow rate, and temperature of the waste water stream.

- How long does it take for the plug to dissolve in a carcass that remains uneviscerated to a point where it is no longer functional to prevent fecal leakage (e.g., line stoppage due to a breakdown or other issue)?

RESPONSE: The plug loses ability to act as a stopper approximately 40 minutes after insertion. See Draft Request for Acceptability Determination at page 9.

- 1% is used as a worst case scenario for residual product left on the intestines. How was that number estimated, i.e., does the notifier have any studies showing what the actual amount of PVOH that remains after washing?

RESPONSE: No amount of PVOH is expected to remain after washing. As noted at page 10 of the GRAS notice, due to the high molecular weight of material (22,000 to 27,000 g/mol), any dissolved PVOH from the plug making direct contact with the inner surface of the bung during slaughter will not penetrate the surface of the intestinal tissue to any significant extent and will be amenable to complete removal through the washing step. Any washing process that is sufficient to remove fecal material (as required for the meat to be considered clean) would also reasonably be expected to remove components of the water-soluble plug. As no data are available to demonstrate that the level of residue is absolutely 0.00% or lower, however, the level of 1% was chosen as a worst-case exaggeration, solely for the purpose of establishing the safety of any unexpected *de minimis* traces of plug material. Based on the weight of a plug (5 grams), this amount (1%) is 50 milligrams (the same weight as about 25 mosquitoes). In this regard, we may assume that such residue would be an intact piece and would be easily visible since the dissolved portion of the plug would be even more likely to be washed away with the fecal material. Accordingly, although the number, 1%, is not based on studies, it surely represents a great exaggeration of the level of PVOH, if any, that may actually remain after washing.

- Polyvinyl alcohol is used in some applications as a binder, for example in consumable tablets. Is there data or scientific literature available to support that PVOH would have no technical effect as a binder at 0.0059%, the estimated highest level remaining in the finished product?

RESPONSE: Polyvinyl alcohol may be used as a *temporary* binder in tablets. Such tablets must be protected from moisture to keep the tablet from dissolving. Thus, PVOH at any level would not be an effective binder in the meat at issue. Further, the level of PVOH necessary for functioning as a binder in consumable tablets appears to be well above 0.0059%. For example, Patent WO2016013675A1 shows tablet formulation using 100 parts of PVOH to 270 parts (combined) of other ingredients, or around 33% PVOH in the tablet. Lower levels of PVOH may have a technical function in other products besides tablets. For example, a product brochure from Millipore indicates that PVOH was studied for use as a thickener in ophthalmic solutions using test samples containing 4%, 10%, and higher concentrations of polyvinyl alcohol. We found no examples of PVOH being used for any technical function at levels lower than 3% (a level at which the Millipore brochure indicates that certain grades of PVOH may help with solubility of the active pharmaceutical ingredient in liquid forms).

Please send the response to the FSIS questions to me, and I will convey to FSIS.

Sincerely,
Paulette Gaynor

Paulette M. Gaynor, Ph.D.
Senior Policy Advisor

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety, Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-1192
Paulette.Gaynor@fda.hhs.gov

From:	Drozen, Melvin S.
To:	Gaynor, Paulette M
Cc:	Alsobrook, Lisa P.
Subject:	FSIS questions for the notifier concerning GRN 000927
Date:	Thursday, August 13, 2020 11:15:23 AM
Attachments:	image001.png image002.png image003.png image004.png image005.png image006.png Acceptability Determination for ADEPT plug and PVOH.docx 25_IM_Slaughter_FS_Standard.pdf 9000.2Rev1.pdf PHVt-Post_Mortem_Inspection.pdf US10028915.pdf

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Dear Dr. Gaynor,

The attached "Draft Request for Acceptability Determination" and the PDFs you have requested of the websites referenced in our August 6, 2020 email are provided in response to your August 7, 2020 email below.

In this regard, we note that FDA was copied on our June 8, 2020 email that provided a courtesy copy of the "Draft Request for Acceptability Determination" to USDA/FSIS. Does your August 7, 2020 request, therefore, indicate that FDA wishes to obtain this material to make it part of the GRAS notice for polyvinyl alcohol (PVOH), which FDA has designated as GRN 000927? If so, will the material be included in the publicly available copy of GRN 927 that is expected to be posted to FDA's online GRAS notice inventory?

We reiterate that no plug component is expected to become a component of food when Adept's water-soluble plugs are used as intended in abattoirs to plug the anus of slaughtered sheep, lambs, and hogs for the purpose of blocking the exit of fecal material to prevent contamination of the carcass by intestinal contents during dressing. In asking the United States Department of Agriculture's (USDA) Food Safety Inspection Service (FSIS) if an acceptability determination is required for the intended use of the plugs, however, Adept has not asserted that any plug component is exempt from the definition of "food additive" in Section 201(s) of the Federal Food Drug and Cosmetic Act as a substance that is reasonably expected to become a component of food under the intended conditions of use. This is because analytical data are not readily available to demonstrate in a quantitative manner that the components are not reasonably expected to become a component of food. In this regard, we believe there already is an established basis for concluding that all components of the plugs aside from PVOH have a suitable FDA food regulatory status for the intended use, as set forth in the "Draft Request for Acceptability Determination."

We look forward to FDA's continued review of this submission and would be happy to answer any questions.

Best regards,

Mel Drozen.

From: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Sent: Friday, August 7, 2020 3:48 PM
To: Drozen, Melvin S. <Drozen@khlaw.com>
Cc: Alsobrook, Lisa P. <alsobrook@khlaw.com>
Subject: RE: FSIS questions for the notifier concerning GRN 000927

Dear Mr. Drozen,

Regarding the response of August 6th (which is below), a few of my colleagues and I discussed this as it refers to material that is not within the GRAS notice. Following up on that discussion, FDA is seeking a copy of the material referred to as the "Draft Request for Acceptability Determination." For completeness, FDA is also requesting copies (e.g., PDFs) of the information referred to on websites.

Thank you,
Paulette Gaynor

Paulette M. Gaynor, Ph.D.
Senior Policy Advisor

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety, Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-1192
Paulette.Gaynor@fda.hhs.gov

From: Alsobrook, Lisa P. <alsobrook@khlaw.com>
Sent: Thursday, August 6, 2020 9:03 AM
To: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Cc: Drozen, Melvin S. <Drozen@khlaw.com>
Subject: FW: FSIS questions for the notifier concerning GRN 000927

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1001 G Street NW, Suite 500 West | Washington, DC 20001
Lisa P. Alsobrook
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From: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Sent: Thursday, July 16, 2020 9:05 AM
To: Drozen, Melvin S. <Drozen@khlaw.com>
Subject: FSIS questions for the notifier concerning GRN 000927

Dear Mr. Drozen,

FSIS has the following questions for the notifier concerning GRN 000927:

- What color is the plug and will it affect disposition of the viscera? That is, is the plug visible to the on-line FSIS inspectors and what effect will it have on their ability to detect contamination or pathological lesions in/on the viscera?

RESPONSE: The plug color is white. Given the speed of the slaughter process (500 or more hogs per hour), the plug would not be expected to have dissolved at the time the viscera are presented for inspection and would be visible to inspectors. Further, the plug is not expected to affect disposition of the viscera because the plug will not contact parts that are examined for contamination or pathological inspection of the viscera. The examples for swine viscera inspection, in the FSIS document, Animal Disposition/Food Safety: Post-mortem Inspection, 3/03/19, Entry Training for Public Health Veterinarian (PHV), do not include steps for any part of the viscera that would contact Adept's water-soluble plugs. Specifically, the PHV Entry Training document states:

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Please send the response to the FSIS questions to me, and I will convey to FSIS.

Sincerely,
Paulette Gaynor

Paulette M. Gaynor, Ph.D.
Senior Policy Advisor

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety, Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-1192
Paulette.Gaynor@fda.hhs.gov

Slaughter Food Safety Standard

Objectives

After completion of this module, the participant will be able to:

1. List the three contaminants covered by the food safety standard in livestock slaughter.

2. Identify the carcass parts that must be free of the three contaminants covered by the livestock food safety standard.

3. Identify the location where FSIS verifies the food safety standard for livestock carcasses.

4. Identify the contaminant covered by the food safety standard in poultry slaughter.

5. Identify the location where FSIS verifies the food safety standard for poultry carcasses.

6. Describe how to perform the livestock zero tolerance verification task.

7. Describe how to perform the poultry zero tolerance verification task.

8. List the actions IPP take when they find a zero tolerance failure during the performance of the poultry and livestock zero tolerance verification tasks.

9. Document zero tolerance verification tasks in PHIS.

10. Describe the enforcement actions when repetitive zero tolerance noncompliance is documented in PHIS.

Introduction

The Food Safety and Inspection Service (FSIS) published in FR 97-067N notification that the Agency views its ‘‘zero tolerance’ for visible fecal material as a food safety standard. In slaughter establishments, fecal contamination of carcasses is the primary avenue for contamination by pathogens including Shiga toxin producing *E. coli* (STECs), *Salmonella*, and *Campylobacter*. These pathogens may reside in fecal material, both in the gastrointestinal tract and on the exterior surfaces of the animal or bird going to slaughter. Without proper handling and sanitary dressing of carcasses during slaughter, the edible portions of the carcass can become contaminated with bacteria capable of causing illness

in humans. The organisms may spread directly from carcass to carcass or indirectly by hands, utensils, or equipment.

Because fecal material is a vehicle for pathogens, and because virtually all slaughter establishments recognize that contamination of meat by pathogenic microorganisms from fecal material, ingesta, or milk is a food safety hazard that is reasonably likely to occur in the slaughter production process, IPP are to verify that slaughter establishments have implemented process controls that are effective in reducing the occurrence of pathogens. To determine the effectiveness of the establishment's controls, FSIS enforces a "zero tolerance" standard for visible fecal material on poultry carcasses and visible fecal, ingesta, or milk material on livestock carcasses, head, cheek, and weasand meat at inspected establishments that slaughter poultry or livestock at a specific point in the process.

Now let's discuss the slaughter food safety standard for livestock and poultry postmortem and how it is verified.

Enforcing Food Safety Standard for Livestock Postmortem

References: FSIS PHIS Directive 6420.2, Regulations: 9 CFR 310.17(a), 310.18(a), and Part 417.

On-Line Livestock (Cattle including Veal, Swine, Sheep and Goat) Inspection

On-line IPP verify the removal of contamination while examining heads, viscera, carcasses, and carcass parts during post-mortem inspection. If on-line IPP observe contamination on heads, viscera, carcasses and carcasses parts, IPP do not pass the carcass or part until all the contamination is promptly removed in a satisfactory manner. IPP verify that livestock slaughter establishments are complying with 310.17(a), and 310.18(a).

310.17(a) states:
Lactating mammary glands and diseased mammary glands of cattle, sheep, swine, and goats shall be removed without opening the milk ducts or sinuses. If pus or other objectionable material is permitted to come in contact with the carcass, the parts of the carcass thus contaminated shall be removed and condemned.

9 CFR 310.18(a) states:
Carcasses, organs, and other parts shall be handled in a sanitary manner to prevent contamination with fecal material, urine, bile, hair, dirt, or foreign matter; however, if contamination occurs, it shall be promptly removed in a manner satisfactory to the inspector.

On-line inspectors inspect carcasses and parts using the livestock inspection procedures outlined in FSIS Directive 6100.2. On-line IPP focus their attention on carcass by carcass or product examination and determine whether or not the establishment is meeting the regulatory requirements in the regulations referenced above.

Carcass Inspection

On-line IPP in livestock establishments inspect each carcass to ensure each carcass and attached parts are free of fecal material, milk, ingesta, urine, bile, hair, dirt, or foreign matter contamination as part of the final rail post-mortem inspection. When on-line inspectors find feces, ingesta, or milk on livestock carcasses, the establishment reexamines and removes all contamination from the entire carcass. **On-line inspectors take a regulatory control action and stop the slaughter line unless**:

- The establishment has provided a rail-out loop; **and**

- The IIC has determined that the establishment's rail-out loop is adequate and operated in a manner to maintain sanitary conditions (i.e., prevents carcass-to-carcass contact or cross contamination due to carcasses accumulating on the rail-out loop)

  Note: The rail-out loop allows the establishment to rail contaminated carcasses off-line for trimming of the carcass off-line. On-line IPP reinspect the railed out carcasses trimmed by the establishment after the establishment places them back on-line before the on-line inspection station.

Additionally, on-line inspectors are to notify the IIC or, if unavailable, other off-line IPP when they believe that:

- An establishment's slaughter or sanitary dressing processes are not under control, for example, when there is repetitive presentation of carcasses contaminated with fecal material, ingesta, or milk at the rail inspection station; or

- An establishment's rail-out procedure is inadequate to prevent carcass accumulation and cross-contamination of other carcasses.

Head Inspection

IPP inspect heads that the establishment has prepared in a sanitary manner and are ready for inspection based on the method of presentation that has been approved by the FLS or IIC. The method may vary with the species of livestock. If the on-line head inspector finds contamination on any surface of the head during

inspection, the on-line head inspector is authorized to stop the line until such contamination is removed and the inspection is completed. Before inspecting and passing the head, the on-line head inspector verifies on-line that the establishment removes the contamination (on-line or off-line) in a safe and sanitary manner. On-line IPP also verify that the establishment properly disposes of heads that do not pass inspection.

On-line head inspectors notify the IIC or, if unavailable, other off-line IPP when they believe that the establishment's slaughter process is not under control (e.g., repeated presentation of heads contaminated with fecal material, ingesta, or milk during postmortem inspection). To determine the effectiveness of the establishment food safety system, off line IPP are to perform a livestock zero tolerance task, sanitary dressing procedure task, and verify other regulatory requirements as needed.

Weasand Meat Inspection

While performing viscera inspection, if the on-line inspector finds contamination on weasand meat during the harvesting step, the on-line inspector is to verify the contamination is removed before the weasand meat can be passed. On-line viscera inspectors notify the IIC or other off-line IPP when they believe that the establishment's slaughter process on the table or at viscera inspection is not under control, e.g., repeated presentation of weasand meat, other parts, or carcasses contaminated with fecal material, ingesta, or milk for postmortem inspection. To determine the effectiveness of the establishment food safety system, off line IPP are to perform a livestock zero tolerance task, sanitary dressing procedure task, and verify other regulatory requirements as needed.

Note: On-line IPP who retain carcasses or carcass parts for veterinary disposition are not to authorize establishment trimming until final inspection by a Public Health Veterinarian (PHV) has been made per 9 CFR 310.3. IPP are to notify off-line IPP or PHV if there are any concerns over the identity, location, or sanitary handling of retained carcasses and associated parts. Retained carcasses and associated parts are identified using devices in 9 CFR 312.6(a). Requirements for inspection facilities, handling of contaminated or retained carcasses and parts, and the reinspection of livestock and poultry carcasses or parts to ensure such carcasses or parts are not adulterated or misbranded are specified in 9 CFR 307.2(g), 310.3, 310.17(a), 310.18(a), 318.2(b) and (d), 381.65(f) and 381.91. **Any retained carcass or part that passes inspection by the PHV is subject to reinspection and zero tolerance verification. Livestock (Cattle including Veal, Swine, Sheep and Goat) Food Safety Standard Verification**

Off-line IPP verify that an establishment has adopted controls in its food safety system that it can demonstrate are effective in reducing the occurrence of pathogens, including the controls that prevent contamination of carcasses and

carcass parts with fecal material, milk and ingesta. Off-line IPP follow instructions, perform verification or inspection tasks, and take enforcement actions as described in FSIS PHIS Directives 5000.1and 5000.6. When off-line IPP verify the adequacy of the establishment's procedures in preventing the contamination of carcasses and head, cheek, and weasand meat with ***fecal material, ingesta, or milk,*** they follow the instructions and verification methods including performing Livestock Zero Tolerance tasks as outlined in FSIS Directive 6420.2.

IPP verify the food safety standard for visible fecal, milk, and ingesta contamination on livestock carcasses at or after the **postmortem rail inspection station** and before any additional trimming, washing, or application of carcass interventions by performing the Livestock Zero Tolerance verification task. The establishment's CCP for pathogen contamination or visible contaminants may be at other locations as supported by the hazard analysis. For example:

- The establishment may locate the CCP after the postmortem rail inspection station.

- In other cases, the establishment may have a CCP prior to the postmortem rail inspection station.

Note: Regardless of the location of the establishment's CCP, FSIS off-line IPP will verify compliance with the livestock zero tolerance food safety standard at or immediately after the rail inspection station and before any additional trimming, washing, or application of any interventions.

Head meat, check meat and weasand meat may be used in the production ground beef products. If the meat from these parts is contaminated; it represents a way of importing pathogens, including *E. coli* O157:H7, other Shiga toxin producing *E. coli* (STECs), and *Salmonella spp.*, into ground beef products. Hence, to reduce the possibility of *E. coli* O157:H7, other Shiga Toxin producing *E. coli* (STECs), and *Salmonella* contamination, establishments must also meet the food safety standard for no visible fecal, milk, or ingesta contamination on head meat, cheek meat, and weasand meat. This verification takes place after the establishment has implemented all of its controls and interventions, and at the point of final packaging or when product is placed in a container for storage which is considered to be the end of the harvesting process.

IPP verify hearts, oxtails, market heads, stomachs, intestines, livers, and other meat by-products not attached to the carcass are clean and harvested in a sanitary manner. These organs are not subject to zero tolerance verification unless they are attached to the carcass. When these carcass parts are contaminated, IPP verify other regulatory requirements such as sanitary dressing 9 CFR 416.1 and 416.4(d) and slaughter HACCP requirements in 9 CFR Part

417 to determine whether the establishment's control measures and sanitary dressing procedures prevent contamination during the production process.

Livestock heads, tails, or other parts attached to the carcass at the final rail are subject to zero tolerance verification and are inspected with the carcass when IPP perform the zero tolerance task.

Livestock parts separated from the carcass and not subject to livestock zero tolerance verification ***are subject to*** slaughter HACCP verification.

Livestock (Cattle including Veal, Swine, Sheep and Goat) Zero Tolerance Verification Task

Frequency of the Verification Task

Off line IPP are to perform the Livestock Zero Tolerance Verification task on carcasses and head, cheek, and weasand meat at a minimum of **one time per slaughter shift.** Each livestock zero tolerance verification task includes examination of not only carcasses but also head, cheek and weasand meat. IPP may verify the slaughter food safety standard on carcasses and head, cheek, and weasand meat at the same or at different times during the shift.

IPP perform additional ***directed*** zero tolerance tasks whenever the establishment's slaughter process and sanitary dressing appear out of control. Off-line IPP make such a determination based on:

- Notification by on-line IPP that there is repetitive presentation of carcasses, heads or viscera contaminated with fecal material, ingesta, or milk during postmortem inspection;

- Observations or findings of insanitary dressing which confirm on-line IPP observations;

- Observations of insanitary dressing made on the slaughter or processing floor (e.g., head boning); or

- Previous findings of zero tolerance noncompliance.

Livestock Carcass Verification

Off-line IPP verify zero tolerance on a pre-determined number of carcasses selected after postmortem inspection and at or after the postmortem rail inspection station but prior to additional trimming, washing, or application of interventions to the carcass. Off-line IPP verify the selected carcasses are not contaminated with visible fecal material, ingesta, or milk. If necessary, IPP retain

the selected carcasses to ensure the establishment does not continue to trim the carcasses while off-line IPP are completing their verification.

Off-line IPP follow the steps below when verifying the establishment's food safety system is controlling fecal material, ingesta, or milk contamination on livestock carcasses during the zero tolerance task.

1. Determine the expected slaughter volume for the shift (i.e., the total number of animals to be slaughtered on the shift).

2. Based on the expected slaughter volume for the shift, determine the number of carcass units (whole carcasses, carcass sides, or equal numbers of hind and forequarters) to be examined depending on what can be done safely and efficiently within a particular establishment and by using the following table. For example, if the table instructs IPP to examine 12 whole carcasses (12 carcass units), they could alternately examine 24 sides or 24forequarters and 24 hind quarters.

Slaughter Volume (# of animals pershift)	# of Carcass Units (1 Unit = whole carcass)	# of Sides
100 or less	2	4
101 to 250	4	8
251 to 500	8	16
More than 500	12	24

   Note: For each zero tolerance task performed, it is not necessary to examine all of these units at the same time.

3. Select the carcass units at or after the **postmortem rail inspection station** for examination on-line **regardless of the location of the establishment's CCP**. IPP select the carcass units for the slaughter food safety standard verification as follows:

   - After trimming of contamination identified by the on-line inspector,
   - After the on-line inspector completes carcass inspection,
   - Before washing of the carcass,
   - Before application of post final rail carcass antimicrobial interventions,
   - Before disassembly of the carcass, and
   - In a random manner.

Note: In certain situations, such as those related to worker safety, the IIC with concurrence of the FLS may develop appropriate alternative or temporary procedures with establishment management for carcass inspection to be properly and efficiently conducted until such deficiencies can be permanently addressed.

4. Examine the outside of the selected carcass units using the same method that on-line IPP use at the postmortem rail inspection station.

   Note: For hide-on veal calves, IPP are to perform zero tolerance on all exposed (i.e., not covered by hide) and internal surfaces

5. Identify fecal material or ingesta using the color and texture characteristics, and milk using the color and consistency characteristics provided in Directive 6420.2 and Attachment 3 of this handout.

6. Keep the PHV-IIC or supervisor aware of the establishment's process control status as needed.

Note: IPP in one-inspector assignments perform livestock zero tolerance verification tasks when acting in the off-line inspector role, i.e., the IPP "changes" roles from "on-line inspector" to "verification inspector" when verifying the slaughter food safety standard. IPP use the same carcass selection criteria described above.

Head Meat, Cheek Meat, and Weasand Meat Verification

As part of each Livestock Zero Tolerance verification task performed, off-line IPP also verify that head, cheek, and weasand meat are not contaminated with visible fecal material, ingesta, or milk when the product is ready for final packaging or to be placed in storage. Off-line IPP follow the steps below when verifying that head meat, cheek meat, and weasand meat are free of feces, ingesta, and milk during the zero tolerance task.

1. Review the HACCP plan.

2. Examine the same amount of product as the establishment has listed in the HACCP plan for its monitoring procedure.

   Note: 9 CFR 417.5(a)(2) requires that the establishment maintain a written HACCP plan, including decision-making documents associated with the selection and development of the CCPs and critical limits, and documents that support both the monitoring and verification procedures selected and the frequency of those procedures. Because the establishment is required to have documents to support the monitoring procedures (amount of product examined), IPP should examine the same amount of product as the

establishment has listed in the HACCP plan for the monitoring procedure. If the establishment does not have documents supporting the monitoring procedures, sample size, and frequency, there is noncompliance with 9 CFR 417.5(a)(2).

3. Select product at the final packaging step or when the product is placed in a container for storage after all of the establishment controls and interventions.

4. Examine all outer surfaces of the product selected for fecal material, ingesta, or milk. Identify fecal material or ingesta using the color and texture characteristics, and milk using the color and consistency characteristics provided in Directive 6420.2 and Attachment 3 of this handout.

Enforcing the Food Safety Standard for Poultry Postmortem

References: FSIS , FSIS Directive 6420.5, FSIS Regulation 381.65(f), and part 417.

Verifying that Establishments Prevent Carcasses Contaminated with Feces from Entering the Chilling System

IPP inspect birds for wholesomeness and verify establishment systems are adequate and effective in controlling food safety hazards and producing safe wholesome product. FSIS enforces a food safety standard of zero for visible ***fecal material*** on poultry carcasses through postmortem inspection and reinspection activities at poultry slaughter establishments.

9 CFR 381.65(f) states:
Official poultry slaughter establishments must develop, implement, and maintain written procedures to ensure that poultry carcasses contaminated with visible fecal material do not enter the chiller. Establishments must incorporate these procedures into their HACCP plans, Sanitation SOPs, or other prerequisite programs.

IPP do not allow poultry carcasses with visible feces to enter the chiller or the chill step. FSIS views preventing carcasses with visible fecal contamination from entering the chilling tank as critical to preventing the cross-contamination of other carcasses.

Note: FSIS Directive 6420.5 and this handout provide instructions for conducting verification activities to determine whether an official establishment is complying with 9 CFR 381.65(f). This directive does not affect or change the requirements associated with the inspection, reinspection, or disposition of poultry carcasses observed to have pathological conditions per 9 CFR 381.81 to 381.93.

Note: Poultry major portions and parts are not subject to poultry zero tolerance verification but are subject to slaughter HACCP verification.

Poultry Zero Tolerance Verification Task

IPP assigned to establishments that operate under Streamlined Inspection System (SIS), New Line Speed Inspection System (NELs), New Turkey Inspection System (NTIS), or Traditional Inspection systems are to perform scheduled and unscheduled Poultry Zero Tolerance verification tasks off line to verify that the establishment is preventing carcasses with fecal material from entering the chiller (9 CFR 381.65(f)).

Frequency of the Verification Task

Off-line IPP are to conduct **at least two** fecal contamination checks for each evisceration line for every shift (i.e., the number of checks will total at least 2 times the number of lines per shift) and as scheduled by the Public Health Veterinarian. For example, in a four evisceration line poultry slaughter establishment, IPP will perform and document 8 poultry zero tolerance verification checks for each shift. In establishments with multiple slaughter lines, IPP may need to schedule directed tasks in PHIS above the routine number of Poultry Zero Tolerance Verification Tasks assigned by PHIS to meet the two fecal contamination checks for each evisceration line for every shift requirement. For example, if the establishment has four lines and two routine zero tolerance verification tasks were already scheduled for the day, then at least six additional zero tolerance tasks should be performed as directed tasks.

Poultry Carcass Verification

Off-line IPP are to verify the establishment's dressing process prevents poultry carcasses with visible fecal contamination from entering the chilling system (air, ice or tank chilling). Off-line IPP follow the steps below when performing poultry zero tolerance verification tasks.

1. Randomly select 10 carcasses using an established FSIS method after the final wash and prior to entering the air or tank chiller.

2. Examine the selected carcasses off line, at either:

    - The pre-chill testing station; or

    - Any location after final trim prior to the chiller tank in establishments operating under traditional inspection.

3. Examine the selected carcasses using the following inspection method:

   - For the outside back – While holding the carcass, with the back of the carcass toward the observer, start at the hock area and observe the hocks, back part of the legs, tail area, back of the carcass and top side of the wings.

   - For the outside front – Turn the carcass and observe the bottom side of the wings, breast, and front part of the legs

   - For the inside – Observe the inside surfaces of the carcass and the abdominal flaps and fat.

   - For the neck flap area – Observe the neck flap and the thoracic inlet area.

4. Identify fecal material using the color, consistency and composition characteristics provided in Directive 6420.5 and in Attachment 1 of this handout.

   Note: For poultry carcasses ingesta found during zero tolerance or FPS verification is “extraneous material” that may contribute to development of insanitary conditions in the chiller; it is not a zero tolerance noncompliance. If ingesta is observed during the zero tolerance task, the establishment should be notified of the finding and remove it from the carcass or part. IPP are to evaluate any findings of ingesta contamination with respect to the establishment’s sanitary dressing and to consider the possible sources of the ingesta contamination when performing their verification activities.

Documentation of Livestock and Poultry Zero Tolerance Verification Results in PHIS

IPP must verify either 9 CFR 310.18(a) or 9 CFR 381.65(f) while performing the zero tolerance task. IPP may also verify any of HACCP regulations in Part 417 while performing the task. After verifying the regulations, off-line IPP document the results in PHIS. IPP select the “review and observation” verification activity radio button on the “Activity” tab of the Inspection Results page for ***each*** zero tolerance task performed.

Documenting Compliance with the Zero Tolerance Task

When IPP ***do not*** observe any fecal material, ingesta, or milk on livestock carcasses or on head, cheek, or weasand meat, or feces on poultry carcasses during the verification, and no other regulatory noncompliance is observed, they select the mandatory regulation and any HACCP regulations they verified on the

"Regulations" tab. IPP mark the zero tolerance task as 'Inspection Completed' at the bottom of the Inspection Results page.

Documenting Noncompliance with the Zero Tolerance Task

If IPP find feces, ingesta, or milk on livestock carcasses or head meat, cheek meat, or weasand meat while performing the livestock zero tolerance verification task, ***or*** find feces on poultry carcasses while performing the poultry zero tolerance verification task, IPP are to:

- Verify regulatory requirements associated with 9 CFR 310.18(a), or 381.65(f) and any HACCP regulations verified during zero tolerance verification task,

- Notify the establishment that a zero tolerance noncompliance with 9 CFR 310.18(a) or 381.65(f) exists. If the zero tolerance finding is on a livestock carcass after the postmortem rail inspection station, or on a poultry carcass after the pre-chill testing station, ***and*** at or past the establishment's zero tolerance CCP, IPP inform the establishment that a deviation from a critical limit has occurred,

- Document the noncompliance on an NR citing 9 CFR 310.18(a) or 381.65(f) *and* 9 CFR 417.2(c)(4) if a deviation from a critical limit has occurred (the establishment failed to adequately monitor at a CCP to ensure compliance with the critical limit),

- For poultry zero tolerance failures include a statement that the establishment is not preventing feces from entering the chiller on the NR,

- Document noncompliance with any additional HACCP regulations that were verified during the zero tolerance task on the same NR, and

- Select the mandatory 9 CFR 310.18(a) or 9 CFR 381.65(f) regulation plus any HACCP regulations that were verified while performing the task on the "Regulations" tab of the Inspection results page.

Note: When IPP determine zero tolerance noncompliance while performing the zero tolerance verification task, they are to perform a Slaughter HACCP Verification task to verify that the establishment performs corrective actions for the affected product in accordance with 9 CFR 417.3(a).

HACCP System Verification after Positive Zero Tolerance Findings

After notifying the establishment of the zero tolerance noncompliance, off-line IPP are to:

- Schedule either a ***directed*** Slaughter HACCP or Operational SSOP Review and Observation verification task in PHIS,
- Indicate “zero tolerance noncompliance” as the reason for performing the directed task in PHIS, and
- Verify the establishment has performed all the required corrective actions in accordance with 9 CFR 417.3(a), 417.3(b), or 416.15(b) and 417.3(b) and is properly implementing its HACCP system.

Which Corrective Actions Requirements Must be Met?

If controls in HACCP plan: When the establishment has a zero tolerance CCP in a HACCP plan, IPP are to verify the establishment has met the **HACCP** requirements in while performing the directed (follow-up) Slaughter HACCP verification task. The establishment has, per **9 CFR 417.3(a):**

- Identified and eliminated the cause of the deviation,
- Ensured that the CCP is under control after the action is taken (e.g., another zero tolerance failure is not likely to be detected if the task were performed again),
- Established measures to prevent recurrence, and
- Ensured that no product that is injurious to health enters commerce.
    - The sampled carcasses are restored to a wholesome, unadulterated condition before they continue on the line or re-enter the chiller (air or tank), and
    - The affected product (carcasses and parts) represented by the sample is safe, wholesome, and not adulterated. This usually involves isolating all product back to the establishment’s last acceptable zero tolerance check and restoring wholesomeness or another “supportable” action.

If controls in SSOP: For poultry establishments that have incorporated procedures for preventing carcasses with visible fecal material from entering the chiller into the Sanitation SOP, IPP are to verify the establishment has met the **SSOP** and the **HACCP unforeseen hazard** corrective action requirements while

performing the directed (follow-up) Operational SSOP Review and Observation verification task. The establishment has, per **9 CFR 416.15(b):**

- Ensured appropriate disposition of contaminated product,
- Restored sanitary conditions, and
- Prevented recurrence of direct contamination or adulteration of products,

And, the establishment has, per **9 CFR 417.3(b):**

- Segregated and held affected product,
    - The affected product usually involves isolating all product back to the establishment's last acceptable zero tolerance check or another "supportable" amount of product.
- Determined acceptability of affected product for distribution,
- Ensured that no product injurious to health enters commerce, and
- Performed a reassessment.

If controls in Prerequisite Program: For poultry establishments that have incorporated procedures for preventing carcasses with visible fecal material from entering the chiller into another prerequisite program, IPP are to verify the establishment has met the **HACCP unforeseen hazard** corrective action requirements while performing the directed (follow-up) Slaughter HACCP verification task. The establishment has, per **9 CFR 417.3(b)**:

- Segregated and held affected product,
    - The affected product usually involves isolating all product back to the establishment's last acceptable zero tolerance check or another "supportable" amount
- Determined acceptability of affected product for distribution,
- Ensured that no product injurious to health enters commerce, and
- Performed a reassessment.

Verify the Establishment's HACCP System Implementation and Recordkeeping

IPP are to use the review and observation, recordkeeping, or both verification components during the Slaughter HACCP or Operational SSOP verification task to verify that the establishment is meeting the regulatory requirements.

IPP may directly observe carcasses (hands-on examination) at the establishment's zero tolerance CCP (9 CFR 417.8), or the point in the process identified in the Sanitation SOP or other prerequisite program; review the establishment's slaughter HACCP plan, Sanitation SOP, or other prerequisite program, and ***observe establishment personnel:***

- Performing the establishment's zero tolerance monitoring procedure at the specified frequency in the plan (9 CFR 417.2 (c)(4), Sanitation SOP (416.13(b)) or other prerequisite program (417.5(a)(1)),

- Performing the establishment's verification, direct observation of monitoring procedure, observing the establishment employee conducting the zero tolerance monitoring procedure at the specified frequency (9 CFR 417.2(c)(7)), or

  Note: The establishment's direct observation of the employee performing the zero tolerance check verifies the individual is finding and correctly identifying all feces, ingesta, or milk on carcasses or parts. Establishment verification procedures also verify carcasses found to be contaminated are restored to wholesome unadulterated state.

- Performing corrective actions (9 CFR 417.3 and/or 416.15)

  Note: The establishment should start corrective actions upon being notified of the zero tolerance failure. For poultry carcass zero tolerance failures, the establishment's corrective actions are likely to address carcasses already in the chiller, about to enter the chiller, the chiller media (if the chiller is a tank), and the carcasses that have exited the chiller.

IPP may **review establishment records** related to its zero tolerance CCP, or the procedures for preventing poultry carcasses contaminated with fecal material from entering the chiller in the Sanitation SOP or other prerequisite program. IPP should seek the answers to the following questions.

1. Does the establishment have documentation that supports the location of the zero tolerance CCP, and the development of the monitoring and verification procedures and frequencies according to 9 CFR 417.5(a)(2) or support for the development of the monitoring and frequencies in the

Sanitation SOP or other prerequisite program according to 9 CFR 417.5(a)(1)?

2. Does the establishment have records that document the results of its zero tolerance monitoring and verification procedures?

3. Does the establishment document all corrective actions performed in accordance with 9 CFR 417.5(a)(3) or 416.16(a)?

Note: IPP are to refer to FSIS Directive 5000.1 for instructions on determining SSOP and HACCP noncompliance.

Documenting the Result of the Slaughter HACCP or Operational SSOP Review and Observation Verification Task in PHIS

When the establishment is in compliance with the regulations, IPP select the mandatory HACCP regulations, or Sanitation SOP regulations, and any other regulation they verified on the “Regulations” tab and mark the task as ‘Inspection Completed’ at the bottom of the Inspection Results page.

If IPP find noncompliance with a HACCP regulation, Sanitation SOP regulation or any other regulatory requirement, they are to notify the establishment and document the noncompliance on an NR citing the appropriate regulation per FSIS Directive 5000.1. For instance, if a poultry establishment has incorporated procedures to prevent carcasses with visible fecal contamination from entering the chiller into the Sanitation SOP, and does not monitor the daily implementation of such procedures, the IPP would issue an NR citing 9 CFR 416.13(c) and 381.65(f).

If a poultry establishment does not have written procedures to prevent carcasses with visible fecal contamination from entering the chiller or has not incorporated the procedures into its HACCP system, IPP are to issue an NR citing 9 CFR 381.65(f).

Note: If IPP find zero tolerance failures on livestock carcasses past the final rail or on poultry carcasses, major portions, or parts at or beyond the pre-chill testing station while performing inspection tasks other than the zero tolerance task (**stumble-on occurrences)**, they are to document the noncompliance under the appropriate PHIS task (Slaughter HACCP or Operational SSOP Review and Observation verification task). IPP are to verify that the establishment implements corrective action that meets the requirements of 417.3(a), 417.3(b), or 416.15(b) and 417.3(b) and that the establishment’s is properly implementing its HACCP system during the performance of this task. Off-line IPP may need to perform a ***directed*** instance of the routine verification task unless the verification task is already scheduled for that day and it has not been completed.

Enforcement

Association of Noncompliance

- If IPP find repeated zero tolerance noncompliance and determine that these findings are from the same cause, the current NR is to be associated with a most recent zero tolerance or related NR.

- For each NR, IPP are to use the NR reporting tools in PHIS to identify previous NRs that might be associated with the current NR. IPP are to refer to the PHIS Users Guide for instructions on how to use the PHIS tools for this purpose. When associating NRs for the same cause, IPP are to follow the methodology set out in FSIS PHIS Directive 5000.1

- If the findings do not show the same cause, IPP are not to associate the NRs.

Note: FSIS PHIS Directive 5000.1 and 6410.1 indicate noncompliance with SPS requirements can be associated to Sanitation SOP or HACCP noncompliance for the same cause including the zero tolerance NRs.

The System Approach in Enforcement

When evaluating the overall effectiveness of the food safety system, IPP have access to the results of any establishment testing and of any monitoring activities that may have an impact on the establishment's hazard analysis (See FSIS Directive 5000.2 and FSIS Directive 5000.6). IPP are to review establishment testing results on at least a weekly basis while performing the PHIS "Review of Establishment Data" task.

When IPP have concerns about whether the documented zero tolerance noncompliance is repetitive and indicative a system failure, the IIC is to consider repeated and associated zero tolerance findings in NRs with other inspection results or establishment records support a need for additional enforcement actions.

The IIC is to factor in any trends of zero tolerance noncompliance with results from HACCP, SSOP, sanitary dressing, and SPS verification. IPP are to also compare any trends in noncompliance as they relate to FSIS and establishment testing. The IIC is to determine whether the findings show that there have been isolated incidents of zero tolerance noncompliance, or if the findings are evidence of a systemic problem with the food safety system.
Such an evaluation is to consider the following:

1. Evidence or lack of evidence that the establishment has implemented all required parts of its HACCP system (e.g., HACCP, SSOP, sanitary dressing, or pre-requisite programs).

2. The rate of HACCP, SSOP, Sanitary Dressing or SPS noncompliance.

    - Compliance with HACCP (9 CFR 417) requirements,

    - Sanitation SOP compliance (FSIS PHIS Directive 5000.1),

    - Sanitation Performance Standard compliance (FSIS PHIS Directive 5000.1), and

    - Sanitary Dressing compliance (FSIS Directive 6410.1)

3. Any trend in the rate of noncompliance over time (increase or decrease).

4. Supporting documentation (9 CFR 417.5(a)(1)) or verification results (9 CFR 417.5(a)(2)) that the establishment's corrective actions and preventive measures (e.g., antimicrobial interventions) are effective or not effective .

5. Relevant laboratory testing results in conjunction with records such as:

    - Any other establishment testing data (FSIS Directive 5000.2 Rev. 2),

    - Generic *E. coli* (or other indicator organism) results from establishment testing or carcasses, or parts that indicate increasing microbial contamination, and

    - FSIS microbiological testing results (e.g. *Salmonella* test results and multiple positive STEC results in raw beef manufacturing trimmings from FSIS routine and follow-up sampling).

6. The association of zero tolerance and related NRs with evidence of inadequate implementation of the food safety system (HACCP, SSOP, Sanitary Dressing, and SPS) or laboratory testing can lead to a determination that the food safety system is less than adequate. If so, the IIC is to alert the Frontline supervisor (FLS) and follow the methodology set out in FSIS PHIS Directive 5000.1, Chapter VI, Rules of Practice 1. Enforcement Actions, to determine the appropriate enforcement action.

Note: Off-line IPP must be aware that zero tolerance noncompliance may be indicative of insanitary dressing procedures prior to final inspection or packaging. IPP need to consider what regulatory requirements can also be verified closer to the source or origin of the contamination.

Attachment 1

Identification of Feces for Poultry

To determine whether an establishment is preventing poultry carcasses with visible fecal material from entering the chilling tank (as required by 9 CFR 381.65(f)), inspection program personnel who examine carcasses must be able to properly identify feces.

Three factors—color, consistency, and composition—are essential in identifying fecal material on the inside or outside of poultry carcasses.

- The color of feces ranges from varying shades of yellow to green, brown, and white.
- The consistency of feces is characteristically semi-solid to a paste.
- The composition of feces may or may not include plant material. Inspection program personnel must take care to distinguish feces from ingesta.
- The color of ingesta varies with the diet.
- The consistency of ingesta is characteristically solid or granular; digestive fluids sometimes are present.
- The composition of ingesta is identifiable plant material.

(9 CFR 381.65(f) does not apply to ingesta. However, inspection program personnel who find ingesta during fecal contamination checks are to notify establishment management to remove ingesta from affected carcasses.)

Attachment 2

Livestock Carcass Examination

Based on the expected slaughter volume for that shift (number of animals), IPP determine the number of carcasses or carcass sides to be examined, using the following table.

Number of Animals Slaughtered	Number of carcasses to be Sampled	Number of sides to be Sampled
100 or fewer	2	4
101 to 250	4	8
251 to 500	8	16
More than 500	12	24

a. Select the appropriate number of carcass units randomly.

b. Examine the selected carcass units using the same systematic technique that inspection IPP use at the post-mortem rail inspection station.

c. IPP performing zero tolerance verification may separately and independently examine the designated number of hind quarters and forequarters to verify the appropriate number of sides or carcasses.

d. IPP may use the above table when slaughtering multiple livestock species provided carcasses are selected randomly.

Attachment 3

Identification of Contaminants for Livestock

To verify the proper removal of contamination from carcasses or carcass parts, IPP assigned to verify that the sanitary dressing procedures are effective must be able to properly identify feces, ingesta, or milk. IPP are to verify the presence of feces, ingesta, or milk by color, texture, and consistency.

The actual appearance of feces and ingesta reflect the diet, age of the animal, type of animal (functioning rumen; non-ruminant)and regional feeding practices. Therefore, the descriptions below are guidelines and are not absolute. The PHV-IIC in each official establishment is the final arbiter regarding any disputed findings of feces, ingesta, or milk representing a zero tolerance noncompliance.

A. Livestock Feces and Ingesta

IPP are to identify foreign material as feces or ingesta based on two factors: color and texture.

<table>
<tr><th colspan="5">Livestock Feces and Ingesta Contamination Identification Chart</th></tr>
<tr><th></th><th colspan="2">Cattle</th><th>Swine</th><th>Sheep and Goat</th></tr>
<tr><td rowspan="2">Color</td><td>Cattle; and Heavy Calf (ruminating)</td><td>Calf (non ruminating)</td><td rowspan="2">Yellow, tan, brown, or green.</td><td rowspan="2">Green, brown, to black</td></tr>
<tr><td>Yellow, green, or brown</td><td>White, yellow, tan</td></tr>
<tr><td>Texture</td><td>Fibrous or plant-like texture; may include grain particles depending on diet.</td><td>Pasty</td><td>May include identifiable grain particles or fibrous plant material.</td><td>Fibrous or plant-like; feces or ingesta may also be tarry.</td></tr>
<tr><td>Size:</td><td colspan="4">The size or quantity of feces or ingesta is largely unimportant in identifying fecal or ingesta contamination. However, as size decreases, color and texture become more difficult to discern.</td></tr>
</table>

NOTE: Bile is a contaminant on carcasses and parts per 9 CFR 310.18 but is not counted as a zero tolerance defect.

B. Milk

Inspection program personnel are to identify foreign material as milk based on two factors: color and consistency.

Milk, if present, tends to be found on the midline, during or after removal of mammary glands (udder) from lactating animals.

Criteria for Identification of Milk on Livestock Carcasses			
	Beef	**Swine**	**Sheep and Goat**
Color	clear to white to light yellow		
Consistency	watery to ropy or curdy		

Workshop: Food Safety Standard in Slaughter

Refer to the handout to complete the following questions.

1. What contaminants are covered by the food safety standard in livestock slaughter?

2. What parts must be free of these contaminants?

3. At what location will FSIS verify the food safety standard for livestock carcasses?

4. Where will FSIS verify the food safety standard for head meat, cheek meat, and weasand meat in livestock slaughter operations?

5. If a livestock slaughter establishment has a CCP for visible contaminants for livestock carcasses at the final washer, where would FSIS verify compliance with the food safety standard?

6. A GS-7 inspector is performing on-line inspection at the rail inspection station in a large beef slaughter establishment. He notices a fecal smear on the hindquarter of a carcass. The establishment has a rail-out procedure.

    a. What action would he take?

    b. What action would he take if the establishment had no rail-out procedure?

    c. What is expected of the establishment?

    d. Would a Noncompliance Record (NR) be completed by the on-line inspector? By the off-line inspector if he or she was functioning as the on-line inspector?

e. If the GS-7 found repeated instances of contaminated carcasses during his time at the rail inspection station, what would he do?

7. A GS-8 off-line slaughter inspector is assigned to a large beef slaughter establishment that kills 2000 head per shift. He is performing a Livestock Zero tolerance verification task to verify compliance with the slaughter food safety standard.

   a. How many **sides** would be selected for examination?

   b. Where, and with what technique, would the sample sides be examined?

   c. If ingesta were found on one carcass side, what action would he take?

8. What contaminants are covered by the food safety standard in poultry slaughter?

9. At what location will FSIS verify the food safety standard for poultry slaughter?

10. If the establishment has a CCP at the antimicrobial rinse after the pre-chill FPS inspection location and just prior to the chiller, where would FSIS verify compliance with the slaughter food safety standard?

11. A new GS-8 off-line slaughter inspector is assigned to a large poultry slaughter operation that has 4 lines and slaughters 160,000 per shift. The establishment has two shifts.

    a. How many fecal contamination checks would need to be performed for one shift including all lines?

    b. How many birds are examined at each check?

    c. How are the birds selected at the pre-chill inspection station?

    d. If she found identifiable fecal material, what actions would she take?

    e. If she does not find any fecal material in any of the checks, what actions would she take?

12. While performing a Poultry Zero tolerance task to verify the slaughter food safety standard on line 2, the IPPfound feces on chicken carcass, verified the establishment corrective actions, and documented noncompliance on an NR. About an hour after the establishment performed corrective actions and restarted line 2; he notices feces on a carcass on line 2 after the washer and prior to the chiller. The establishment tells him since this fecal contamination finding was not part of the Poultry Zero tolerance verification task, his finding was not a slaughter food safety standard (zero tolerance) failure.

    Note: The establishment has incorporated written procedures that prevent poultry carcasses contaminated with visible fecal material from entering the chiller into a HACCP plan).

    a. Is the establishment correct?

b. Is there noncompliance? If so, what inspection task should be used to document the noncompliance?

c. If you determine that there is noncompliance with the regulatory requirements, what regulations should be cited on the NR?

13. How do off-line IPP determine the amount of product to inspect when performing the Livestock Zero Tolerance verification task in a livestock slaughter establishment to verify that the meat from heads, cheeks, and weasands are not contaminated with fecal material, ingesta, or milk?

Zero Tolerance Verification Task Hands-on Exercise

General Instructions

- Read the General information and answer the question,
- Schedule the directed poultry fecal zero tolerance verification tasks on the task calendar,
- Read each scenario and document the result of the poultry zero tolerance verification task in PHIS based on the findings, and
- Schedule a Slaughter HACCP verification task to document your verification of the establishment compliance with all parts of 417.3(a) and that the establishment is properly implementing its slaughter HACCP system.

Establishment Information

You are **Cindy Soundly** the off line IPP assigned to Novosibar which is a poultry slaughter establishment. Novosibar operates two 8 hour shifts, 5 days a week. The establishment has 4 evisceration lines but only two lines are operating on the day shift today. You decide to schedule one poultry zero tolerance task as routine and the remainder as directed.

Note: The establishment has incorporated written procedures that prevent poultry carcasses contaminated with visible fecal material from entering the chiller into its HACCP plan, i.e., it has zero tolerance CCP).

How many directed instances of the routine poultry zero tolerance task should be scheduled for today?

Schedule Poultry Zero Tolerance Tasks in PHIS

Add the one routine task and the number of directed poultry zero tolerance verification tasks that should be scheduled for today to the task calendar.

Use the PHIS Quick Reference GUIDE as needed.

Poultry Zero Tolerance Verification Task Scenarios

Scenario 1: The Routine and One of the Directed Task Findings

At approximately 8:10 a.m., you randomly selected 10 birds from line 1 for the routine task and at approximately 8:40 a.m. you randomly selected 10 birds from line 2 for the first directed task. You examined the carcasses at the pre-chill finished product standards station. You did not observe any identifiable fecal material on the poultry carcasses during your verification, and no other regulatory noncompliance was observed.

Scenario 2: Second Directed Task Findings

At approximately 11:25 a.m., you randomly selected 10 birds from line 1. You examined the carcasses at the pre-chill finished product standards station. In the neck area of the 3rd carcass selected, you observed a ½ inch by ¼ streak of yellowish granular material. In the same area of 8th carcass selected, you observed a ¾ inch by ¼ streak of greenish granular material. You determine that these defects are ingesta and notify the kill floor supervisor, Mr. Hurbert Jones. The ingesta was trimmed from the carcasses. You did not observe any identifiable fecal material on the poultry carcasses and no other regulatory noncompliance was observed.

Scenario 3: Third Directed Task Findings

At approximately 1:00 p.m., you randomly selected 10 birds from line 2. You examined the carcasses at the pre-chill finished product standards station. On the outside back of the 7th carcass selected, you observed a ½ inch by ¼ brown pasty smear with plant material. You determine that the defect is fecal material. You notify the establishment kill floor supervisor, Mr. Hurbert Jones, and the evisceration supervisor, Jane Fontana, of the fecal contamination. Mr. Jones is shown the contamination and states “this is ingesta not feces“. Your supervisor PHV-IIC, Dr. Phyllis Isaacs, is shown the carcass and confirms the fecal contamination finding. You observe Ms. Fontana remove the contaminated carcass and take it to reprocessing where it was rinsed with 20-30 ppm chlorinated water.

You stay in the area while the establishment performs corrective actions on the remaining affected product. Ms. Fontana determined that the vent machine was out of adjustment and the following corrective actions were taken.

- Maintenance stopped the line to readjust the vent machine;
- All product between the vent machine (after it was readjusted) and the chiller was retained for reconditioning and reprocessing;
- The overflow in the chill system for the carcasses was increased;
- The level of chlorine in the chiller was increased from 20 ppm to 40 ppm;
- All surfaces of the carcasses from the last acceptable monitoring check (approximately 40 minutes of production) were rinsed with 20-30 ppm chlorinated water; and
- After the line was restarted, a QC technician sampled and examined carcasses entering the chill system for visible fecal material.

Scenario 4: The Slaughter HACCP Verification Task

Schedule the Slaughter HACCP Verification Task

Since the establishment has a zero tolerance CCP in their HACCP plan, and IPP find identifiable fecal material on a carcass or carcass part while performing a Poultry Zero Tolerance task, IPP are to perform a ***directed*** Slaughter HACCP verification task to verify the establishment has performed all required HACCP corrective actions per 9 CFR 417.3(a) and is properly implementing its Slaughter HACCP system.

Schedule a directed Slaughter HACCP verification task. Use “zero tolerance noncompliance” as the justification.

Task Findings

You directly observed some of the establishment’s corrective actions at the time the establishment implemented them (see scenario #3 above). Near the end of the shift, you review the establishment’s corrective action record in the HACCP coordinator’s office. In addition to the corrective actions you observed above, you find the following entries.

- Maintenance personnel will inspect the functioning of the vent machine at first break; lunch and second break for each shift and make adjustments as needed. The result of each check will be documented on the fecal monitoring record.

- Three fecal checks instead one check were performed per clock hour for the remainder of the shift. The additional fecal checks were documented on the fecal monitoring record.

You ask the HACCP coordinator for the fecal monitoring record for the shift. He gives you all of the monitoring records for the shift which includes the chlorine log for the chilling CCP. You note that the establishment documented 6 fecal checks

for the last 2 hours for the shift. In addition, you see that the establishment has documented the vent machine check for the second break. You decide to review all the monitoring entries on the both the fecal and chlorine records. The establishment is monitoring at the frequency stated in the HACCP plan and the results are within the critical limit for each CCP.

Note: Before this task can be completed, you must verify the monitoring, verification, corrective action, and recordkeeping requirements at all CCPs for the specific production.

Document the Inspection Results of the Zero Tolerance Tasks and Slaughter HACCP Verification Task in PHIS

Working independently, log back into the PHIS computer and document the inspection results, you will:

- Document the inspection result for each of the poultry zero tolerance verification task. Include any inspector notes.
- If noncompliance is found, document the noncompliance on an NR,
- Finalize the NC and complete the NR, if possible,
- Complete the Task, if possible, and
- Document the result of the Directed Slaughter HACCP Verification Task

Use the PHIS Quick Reference Guide as needed.

UNITED STATES DEPARTMENT OF AGRICULTURE
FOOD SAFETY AND INSPECTION SERVICE
WASHINGTON, DC

FSIS DIRECTIVE

9000.2
Revision 1
7/30/10

INSPECTION AND EXPORT CERTIFICATION OF LIVESTOCK INTESTINES OR CASINGS

I. PURPOSE

This directive instructs inspection program personnel (IPP) how to determine whether intestines or casings from livestock are eligible to receive the mark of inspection and how to certify eligible intestines or casings for export.

Key Points Covered

- explains how to determine whether intestines or casings are eligible to receive the mark of inspection;

- instructs IPP on what is required to certify intestines or casings for export;

- instructs IPP on what is required to certify imported intestines or casings for export;

- contains Questions and Answers for The Inspection and Export Certification of Livestock Intestines (Attachment 1). The Food Safety and Inspection Service (FSIS) may post additional Questions and Answers on askFSIS.

II. CANCELLATIONS

FSIS Directive 9000.2, Inspection and Export Certification of Livestock Intestines or Casings, dated 10/27/08

III. REASON FOR REISSUANCE

This directive clarifies that FSIS does not expect imported casings that are to be certified for export with FSIS Form 9060-18 to have been derived solely from livestock that was slaughtered under an inspection system equivalent to the U.S. system.

IV. REFERENCES

9 CFR 310.22
9 CFR Parts 96.3, 322, and 350
FSIS Directive 6100.4, "Verification Instructions Related to Specified Risk Materials"
FSIS Directive 6420.2, "Verification of Procedures for Controlling Fecal Material, Ingesta and Milk in Slaughter Operations"
FSIS Directive 9000.1, "Export Certification"
FSIS Directive 12,600.1, "Voluntary Reimbursable Inspection Services"

V. BACKGROUND

A. Since June 2006, FSIS has issued a series of notices designed to bring the inspection and certification services that FSIS performs on a fee-for-service basis under 9 CFR Part 350, Special Services Relating to Meat and Other Products, in line with other inspection activities that the Agency performs, particularly those that may result in the application of the mark of inspection.

B. Products labeled as "(species) intestines" are meat byproducts derived from the intestines of livestock and, as such, are under FSIS jurisdiction. Therefore, products labeled "(species) intestines" are required to be produced under inspection and are eligible to bear the mark of inspection.

C. Products labeled as "(species) casings" are derived from the intestines of livestock and are used as containers to prepare sausage and other meat food products. Casings are under the jurisdiction of the Food and Drug Administration (FDA) and normally do not bear the mark of inspection. A non-FSIS inspected facility (a casing manufacturer) may request voluntary reimbursable service under 9 CFR 350.3 to prepare casings under FSIS inspection, thus making them eligible to bear the mark of inspection.

D. Beef distal ileum is a specified risk material (SRM) in all ages of cattle and must be disposed according to 9 CFR 310.22(a)(2) and 310.22(c) prior to leaving inspection oversight at the slaughter establishment.

VI. INSPECTION PROGRAM PERSONNEL VERIFICATION ACTIVITIES AT OFFICIAL ESTABLISHMENTS PREPARING INTESTINES OR CASINGS

A. Intestines or casings prepared at official establishments are eligible to bear the mark of inspection and can be certified for export, provided, they are produced under sanitary conditions resulting in clean, wholesome, not adulterated, and properly labeled product.

B. IPP are to consider the intestines or casings clean when they are visibly free of digestive tract contents. Intestines or casings are not subject to a zero tolerance standard for ingesta and fecal material. The zero tolerance standard applies to livestock carcasses and parts only (FSIS Directive 6420.2).

C. IPP are to verify that the intestines or casings are suitable for the intended use of the product. To receive the mark of inspection, the intestines or casings must be in an appropriate condition and suitable for use as an edible product.

D. Intestines or casings prepared at an official establishment are not required to bear the mark of inspection. When requested by establishments, IPP are to allow official establishments to prepare and ship intestines or casings that do not bear the mark of inspection and without denaturing the intestines, provided the process does not cause adulteration of edible product or produce unsanitary conditions, and the product is suitable for its intended purpose. After removal of the distal ileum from bovine intestines, the remaining intestines may leave the establishment undenatured as inspected or uninspected product.

VII. EXPORT CERTIFICATION OF INTESTINES OR CASINGS AT AN OFFICIAL ESTABLISHMENT

A. When requested, at an official establishment, IPP are to certify intestines or casings for export (see FSIS Directive 9000.1, Revision 1, "Export Certification") as a non-reimbursable service in accordance with 9 CFR Part 322.

B. IPP are to provide the certification service and permit the application of approved labels bearing the mark of inspection to intestines or casings prepared from livestock slaughtered, inspected, and passed at that establishment or at another official establishment.

C. When an importing country requires certification of requirements not imposed by FSIS meat and poultry regulations, IPP are to certify intestines and casings for export (when requested) as a reimbursable service in accordance with 9 CFR 350.3(b).

VIII. EXPORT CERTIFICATION OF CASINGS AT A CASINGS FACILITY

A. When requested, IPP are to certify casings for export (see FSIS Directive 9000.1, Revision 1, "Export Certification") as a reimbursable service in accordance with 9 CFR 350.3.

B. If a casings facility requests FSIS certification service for domestic casings not bearing the mark of inspection, IPP are to sign the Export Certificate, FSIS Form 9060-7 (08/13/2008), "Animal Casings Export Certificate for Countries Requiring Ante-Mortem, Post-Mortem, and Fit for Human Food Statements,"provided IPP are able to certify that all the statements in the certification, including the following statement, are factual based on the documentation accompanying the shipment:

> *I certify that the animal casings specified hereon were derived from animals which received USDA ante-mortem and post-mortem veterinary inspection at the time of slaughter, and that the casings are sound, healthful, wholesome, and otherwise fit for human food. While in establishments subject to USDA inspection, said casings have been handled in a sanitary manner and were not subject to contagion prior to exportation.*

C. Such casings are not eligible for the mark of inspection. The documentation is to substantiate that the intestines were harvested under sanitary conditions from livestock that passed ante-mortem and post-mortem inspection in the United States (U.S.) and meet the requirements listed in the Export Library for the importing country. Export requirements for destination countries can be found at

http://www.fsis.usda.gov/regulations_&_policies/Export_Information/index.asp.

D. FSIS Form 9060-7 is used for the export of casings derived from livestock slaughtered under USDA inspection, regardless of where the casings were further processed. IPP can sign FSIS Form 9060-7 even when the casings do not bear the mark of inspection or were processed outside of the U.S., provided they are presented with evidence that the animals were slaughtered under inspection in the U.S.

E. Casings processed outside of the U.S. must be accompanied by the documentation described in IX below and all documentation provided to FSIS inspection personnel is to be written in English.

F. When requested by a casings facility, the application of the mark of inspection will be granted as a reimbursable service, provided the casings were derived from intestines that received the mark of inspection. The casings must not have been processed outside the U.S. Casings processed outside the U.S. are not eligible for the mark of inspection.

IX. EXPORT CERTIFICATION OF IMPORTED CASINGS

A. Imported casings are regulated by FDA. Therefore, FSIS IPP do not inspect imported casings or permit the application of the USDA mark of inspection to them. However, IPP can certify imported casings for export.

B. When requested, IPP are to certify imported casings for export (see FSIS Directive 9000.1, Revision 1, "Export Certification") as a reimbursable service in accordance with 9 CFR 350.3.

C. IPP are to provide export certification to imported casings, provided that the casings in the shipment presented are clean and sound

D. IPP also are to verify that:

1. The imported casings are accompanied by a certificate signed by a government official of the exporting country stating:

> *I hereby certify that the animal casings herein described were derived from healthy animals (cattle, sheep, swine, or goats), which received ante-mortem and post-mortem veterinary inspection at the time of slaughter, are clean and sound, and were prepared and handled only in a sanitary manner and were not subjected to contagion prior to exportation.*

2. There is documentation in English from an official of the exporting country stating that the casings have not been commingled with casings from non-inspected sources, and documentation showing that the casings were released by U.S. Customs and Border Protection.

NOTE: The Animal and Plant Health Inspection Service requires this certificate in accordance with 9 CFR 96.3.

E. IPP are to ensure that the country to which the casings are to be exported does not restrict the importation of casings (i.e., the Export Library does not state "only casings originating from the U.S. are eligible," or similar wording). IPP are to verify that any requirements of the Export Library related to the shipment are met.

F. If requested by an exporter, IPP are to sign FSIS Form 9060-18 (08/13/2008), "Animal Casings Export Certificate for Countries Requiring Ante-mortem, Post-mortem, and Sound and Clean Statement," if, based on all of the documentation accompanying the shipment, they are able to make the following statement,

> *I certify that the animal casings specified hereon were accompanied by documentation showing they were derived from healthy animals which received ante-mortem and post-mortem veterinary inspection at the time of slaughter, and are clean and sound. While in establishments subject to USDA inspection, said casings have been handled in a sanitary manner and were not subject to contagion prior to exportation.*

G. Facilities may re-pack and re-label imported casings (without the USDA mark of inspection) under voluntary inspection, and FSIS Form 9060-18 may be used for the export of the casings, regardless of where the casings were further processed. FSIS Form 9060-18 can be issued only if all of the casings in a shipment presented for export certification are accounted for in the facility's documentation and meet the conditions described above.

Refer questions to the Policy Development Division at 1-800-233-3935 and follow the auto- attendant menu prompts for questions regarding export of casings. Alternatively, submit technical questions through askFSIS.

Assistant Administrator
Office of Policy and Program Development

Attachment 1

QUESTIONS AND ANSWERS FOR THE INSPECTION AND EXPORT CERTIFICATION OF LIVESTOCK INTESTINES

Q1. The directive states that intestines or casings should be considered clean when they are "visibly free of digestive tract contents", but that some small amount of digestive tract material may still adhere to the intestine or casing. How will inspection program personnel (IPP) be able to determine whether the intestines or casings are clean?

A1. IPP are to verify that the establishment demonstrates good process control in cleaning intestines and makes reasonable efforts to remove contamination during cleaning and other processing of the product. No significant amount of fecal material or other contamination should remain on or in the intestine, although some small amount of digestive tract material may adhere to the intestine (mainly the intestinal mucosal lining) even after a reasonable effort to clean it has been made. The presence of such material should not cause IPP to withhold the mark of inspection. IPP are to make their determinations of the acceptability of product to bear the mark of inspection based on production lots and process controls rather than on individual units of product.

Q2. Does the mucosa (on the inner surface of the intestine) need to be stripped away for the intestine to be "visibly free of digestive tract contents?"

A2. No. The establishment does not have to strip the mucosa from the intestines for them to be given the mark of inspection.

Q3. Are intestines that are intended to be processed into casings required to bear the inspection legend prior to leaving an official establishment?

A3. No. Establishments may prepare and ship in commerce intestines without the mark of inspection.

Q4. Are livestock casings used in preparing meat or poultry food products in federally-inspected establishments required to bear the USDA mark of inspection?

A4. No. The directive does not change any policy regarding the use of casings when preparing other inspected products. Casings used to make meat or poultry food products in federally-inspected establishments are not required to bear the USDA mark of inspection because livestock casings are regulated by FDA as containers. Casings used in preparing meat and poultry in federally-inspected establishments must comply with 9 CFR 318.6 (b) (1), (2), and (3).

Q5. Does the directive apply to any portion of the livestock digestive tract used to produce casings?

A5. Yes. The directive applies to any part of the digestive tract of livestock, including stomachs (maws), small intestines (rounds), anterior and distal ceacum (bung/cap), large intestine (middles), rectum (bung/straight casing), or bladder, provided they meet the conditions set forth in this directive.

Q6. Are non-official establishments able to process intestines (for preparation into casings) and casings for export as an FDA product?

A6. Yes, as FDA products.

Q7. If a casings processing firm leases a non-inspected room in a federally-inspected establishment, could it process the intestines produced in that establishment, or another federally-inspected establishment, into casings for export certification under voluntary reimbursable inspection in that room?

A7. Yes. The firm may request voluntary reimbursable service to provide inspection for casings processing under 9 CFR 350.3, in order to apply the USDA mark of inspection to the casings. As mentioned above, FDA regulates casings. Therefore, when firms request the USDA mark of inspection for export certification of casings, the inspection of the processing and preparation is a reimbursable service under 9 CFR Part 350. The firm requesting this voluntary reimbursable service must apply to the District Manager (DM) using FSIS Form 5200-6, "Application Approval for Voluntary Reimbursable Inspection Service," (see FSIS Directive 12,600.1, Revision 1, "Voluntary Reimbursable Inspection Services.") The DM may assign a separate number for the voluntary service, or the firm may use the same number as the establishment in which it operates.

Q8. If a U.S. slaughter establishment harvests intestines from livestock that have passed ante-mortem and post-mortem inspection at the establishment, can the establishment ship the partially-cleaned intestines, without the mark of inspection, to a second establishment for further processing into casings that will be certified later for export?

A8. Yes. A slaughter establishment can harvest intestines from livestock that have passed ante-mortem and post-mortem inspection and ship those intestines only partially cleaned to another facility or establishment for further preparation into casings. Copies of the records are to accompany the shipment of the product in order to maintain its identity. Establishments may use company seals or have the product move under FSIS control (e.g., USDA seal, accompanied by FSIS Form 7350-1, "Request and Notice of Shipment of Sealed Meat/Poultry") while it is in transit. Labels for these intestines should bear a statement of limited use designating what is being done to them and their destination for further processing.

Q9. Can the distal ileum of a beef intestine be removed at another establishment when the intestine is further cleaned?

A9. No. As provided in 9 CFR 310.22(c), SRMs must be removed and disposed of under inspection oversight at the slaughter establishment.

Q10. Who is responsible for costs involved in export certification of casings and intestines?

A10. The firm requesting the export certification is responsible for the expenses associated with export certification.

Q11. Are HACCP plans required for preparing casings as food articles under 9 CFR Part 350?

A11. No. Preparing casings under Part 350 is a voluntary reimbursable service, which does not require a HACCP plan. IPP are responsible for verifying that the product produced is not adulterated, and that the facilities meet the sanitary performance standards outlined in 9 CFR 416.1-6. For additional information on voluntary reimbursable services, see FSIS Directive 12,600.1, Revision 1. In contrast, intestines labeled as "(species) intestines" are meat byproducts. Therefore, if an establishment prepares and labels "(species) intestines," that process needs to be considered in the establishment's hazard analysis, and any hazards reasonably likely to occur are to be addressed in its HACCP plan.

Q12. Do labels for "(species) casings" prepared under voluntary reimbursable service (9 CFR Part 350) and intended for export need to be approved by FSIS, i.e., the Labeling and Program Delivery Division (LPDD)?

A12. Yes. Companies need to submit labels for "(species) casings" prepared under 9 CFR Part 350 for export to LPDD for approval. Deviations from domestic labeling rules are permitted in accordance with 9 CFR 317.7. The label application should contain documentation that supports the receiving country's acceptance of the deviation. However, labeling for casings that do not bear the mark of inspection or statements of limited use is not required to be submitted to the LPDD for approval.

Post-mortem Inspection

OBJECTIVES

1. Define the purpose of post-mortem inspection.
2. Identify the statutes that provide FSIS the authority for conducting post-mortem inspection.
3. Identify the regulations that cover post-mortem inspection.
4. List the Directives that provide instructions on conducting post-mortem inspection procedures.
5. Identify the establishment responsibilities with regard to conducting post-mortem inspection.
6. Describe the process of conducting post-mortem inspection procedures.
7. Define how the establishment must dispose of condemned product.
8. Describe how to complete post-mortem reports.

INTRODUCTION

Post-mortem inspection covers the inspection of the carcasses and parts of meat and poultry used for human food. It takes place after ante-mortem inspection and after the animal or poultry has been slaughtered thus the term “post-mortem,” meaning “after death” in Latin. Post-mortem inspection covers the steps in the slaughter process that begin at stunning and ends at the step where the carcass is placed in the cooler.

The purpose of post-mortem inspection is to protect the public health by ensuring that the carcasses and parts that enter commerce are wholesome, not adulterated, and properly marked, labeled, and packaged. This means that any carcasses or parts that are unwholesome or adulterated, and thereby unfit for human food, do not enter commerce. In performing inspection methods, making regulatory decisions, documenting findings, and taking enforcement actions when appropriate, in relation to post-mortem inspection we are guided by the following statutes, regulations, directives, and notices.

If you are assigned to work in a large establishment, you will be supervising inspectors who perform the post-mortem inspection procedures. However, it may be necessary for you to perform the post-mortem inspection procedures for the inspectors while they take their breaks. If you are assigned to work in a very small establishment, you may be performing some or all of these procedures.

<u>Statutes covering post mortem inspection</u>

The statutory authority for post-mortem inspection is as follows.

Livestock:

FMIA Section 604. *“Post-mortem examination of carcasses and marking or labeling; destruction of carcasses condemned; reinspection. For the purposes hereinbefore set*

forth the Secretary shall cause to be made by inspectors appointed for that purpose a post-mortem examination and inspection of the carcasses and parts thereof of all cattle, sheep, swine, goats, horses, mules, and other equines to be prepared at any slaughtering, meat canning, salting, packing, rendering, or similar establishment in any State, Territory, or the District of Columbia as articles of commerce which are capable of use as human food; and the carcasses and parts thereof of all such animals found to be not adulterated shall be marked, stamped, tagged, or labeled as "Inspected and passed;" and said inspectors shall label, mark, stamp, or tag as "Inspected and condemned" all carcasses and parts thereof of animals found to be adulterated; and all carcasses and parts thereof thus inspected and condemned shall be destroyed for food purposes by the said establishment in the presence of an inspector, and the Secretary may remove inspectors from any such establishment which fails to so destroy any such condemned carcass or part thereof, and said inspectors, after said first inspection, shall, when they deem it necessary, reinspect said carcasses or parts thereof to determine whether since the first inspection the same have become adulterated, if any carcass or any part thereof shall, upon examination and inspection subsequent to the first examination and inspection, be found to be adulterated, it shall be destroyed for food purposes by the said establishment in the presence of an inspector, and the Secretary may remove inspectors from any establishment which fails to so destroy any such condemned carcass or part thereof."

Poultry:

PPIA Section 455(b). *"Post-mortem inspection: quarantine, segregation, and reinspection. The Secretary, whenever processing operations are being conducted, shall cause to be made by inspectors, post-mortem inspection of the carcass of each bird processed, and at any time such quarantine, segregation, and reinspection as he deems necessary of poultry and poultry products capable of use as human food in each official establishment processing such poultry or poultry products for commerce or otherwise subject to inspection under this chapter."*

<u>Regulations covering post-mortem inspection</u>

The regulations that cover post-mortem inspection for livestock are as follows.

- 9 CFR 310.2 – States that the establishment must have a system that is used to identify livestock carcasses and parts to be used in the preparation of meat food products or in medical products (e.g., head, tail, tongue, thymus, viscera, blood, and other parts) as being derived from the particular animal involved until the post-mortem inspection of the carcass and parts is completed.

- 9 CFR 310.3 – States that any carcasses, organs, or parts in which any lesion or other condition is found that might render the meat or any part unfit for human food, or otherwise adulterated must be retained for veterinary disposition. The identity of the carcass, organs, and parts must be maintained until final disposition has been completed. Retained carcasses shall not be washed or trimmed unless authorized by FSIS.

- 9 CFR 310.4 – Identifies that U.S. Retained tags will be used to temporarily identify any carcasses, organs, or parts retained for veterinary disposition. These tags can only be removed by an FSIS employee.

- 9 CFR 310.5 – States that any carcass or part found upon final inspection to be unsound, unhealthful, unwholesome, or otherwise adulterated shall be conspicuously marked as U.S. Condemned. These carcasses or parts must remain in the custody of FSIS and disposed of according to the regulations before the close of the day upon which they are condemned.

- 9 CFR 310.6 – States that carcasses and parts that are passed for cooking only shall be marked U.S. Passed for Cooking, and must remain in the custody of FSIS until they are cooked according to 9 CFR 315.

- 9 CFR 310.8 – Describes passing and marking carcasses and parts. Those that are found to be sound, healthful, wholesome and otherwise not adulterated are marked U.S. Inspected and Passed. Those that show localized lesions are passed for food or for cooking, and the U.S. Retained tag is attached until the affected tissue is removed and condemned.

- 9 CFR 310.18(a) — States that *"carcasses, organs, and other parts shall be handled in a sanitary manner to prevent contamination with fecal material, urine, bile, hair, dirt, or foreign matter; however if contamination occurs it shall be promptly removed in a manner satisfactory to the inspector".*

- 9 CFR 310.21 – Covers residues in post-mortem inspection. We will address this in a separate section of the training.

- 9 CFR 310.25 – Covers contamination of livestock carcasses and parts with microorganisms; process control verification criteria and testing; and pathogen reduction standards. You will learn about this is more detail when you attend the Inspection Methods class.

- 9 CFR 311 – Covers diseased and otherwise adulterated carcasses and parts. You will learn more details about the specific diseases and disposition principles in the module called Multi-Species Dispositions.

- 9 CFR 314 – Covers how establishments must handle condemned and inedible carcasses and parts.

- 9 CFR 315 – Covers rendering or other disposal of carcasses and parts, and product that has been passed for cooking during post-mortem inspection.

The regulations that cover post-mortem inspection for poultry are as follows.

- 9 CFR 381.76 – Covers post-mortem inspection procedures for five systems: traditional systems, Streamlined Inspection System (SIS), New Line Speed (NELS) Inspection System, the New Turkey Inspection (NTI) System, and the Ratite Inspection System. Section 381.76(a) states that *"a post-mortem inspection shall be made on a bird-by-bird basis on all poultry eviscerated in an official establishment."* Section 381.76(b) outlines the inspection procedures for each of these four inspection systems. It includes responsibilities of the establishment helper and trimmers, and requirements of establishment facilities. It also defines the maximum inspection rate, which is the line speed that is

allowed for each inspection system. Inspection procedures and actions are outlined, as well as reinspection duties.

- 9 CFR 381.77 – Covers carcasses held for further examination. It indicates that each carcass or any parts in which there is a lesion of disease or other condition which might render it adulterated and with respect to which a final decision cannot be made upon first examination by the inspector shall be held for further examination. The identity of the carcass and all parts must be maintained until a final examination has been completed.

- 9 CFR 381.78 – Covers condemnation of carcasses and parts; and separation of poultry suspected of containing biological residues. Section 381.78(a) states that at any time during inspection a carcass or part is found to be adulterated, it shall be condemned, except any articles that may be made not adulterated by reprocessing if reprocessed under the supervision of an inspector and then found to be not adulterated. Section 381.78(b) states that *"when a lot of poultry suspected of containing biological residues is inspected in an official establishment, all carcasses and any parts of the carcasses in such lot which are condemned shall be kept separate from all other condemned carcasses or parts."*

- 9 CFR 381.79 – States that *"each carcass and all organs and other parts of carcasses which are found to be not adulterated shall be passed for human food."*

- 9 CFR 381.80 – Addresses biological residues. Section 381.80(a) states that the carcasses or parts found during post- mortem inspection or at any subsequent inspection to be affected with any diseases or conditions named in other sections of this subpart shall be disposed of in accordance to the section that pertains to the disease or condition. It states that because it is impractical to formulate rules for all diseases or conditions, the decision as to the disposal of all carcasses, organs, or other parts will be left to the inspector in charge, and if the inspector in charge is in doubt of the disposition to be made, he or she shall forward specimens from the carcasses to the laboratory for diagnosis. Section 381.80(b) states that all carcasses, organs, and parts shall be condemned if it is determined on the basis of a sound statistical sample that they are adulterated because of the presence of any biological residue.

- 9 CFR 381.81 – States that *"carcasses of poultry affected with tuberculosis shall be condemned."*

- 9 CFR 381.82 – States that *"carcasses of poultry affected with any one or more of the several forms of the avian leukosis complex shall be condemned."*

- 9 CFR 381.83 – States that *"carcasses of poultry showing evidence of any septicemic or toxemic disease, or showing evidence of an abnormal physiologic state, shall be condemned."*

- 9 CFR 381.84 – States that *"carcasses of poultry with evidence of extensive involvement of the air sacs with airsacculitis or those showing airsacculitis along with systemic changes shall be condemned. Less affected carcasses may be passed for human food after complete removal and condemnation of all affected tissues including the exudate."*

- 9 CFR 381.85 – States that *"carcasses of poultry showing evidence of any disease which is characterized by the presence, in the meat or other edible parts of the carcass, or organisms or toxins dangerous to the consumer, shall be condemned."*

- 9 CFR 381.86 – States that *"any organ or other part of a carcass which is affected by an inflammatory process shall be condemned and, if there is evidence of general systemic disturbance, the whole carcass shall be condemned."*

- 9 CFR 381.87 – States that *"any organ or other part of a carcass which is affected by a tumor shall be condemned when there is evidence of metastasis or that the general condition of the bird is found to have been affected by the size, position, or nature of the tumor, the whole carcass shall be condemned."*

- 9 CFR 381.88 – States that *"organs or other parts of carcasses which are found to be infested with parasites, or which show lesions of such infestation shall be condemned and, if the whole carcass is affected, the whole carcass shall be condemned."*

- 9 CFR 381.89 – States that *"any part of a carcass which is badly bruised shall be condemned and, if the whole carcass is affected as a result of the bruise, the whole carcass shall be condemned. Parts which show only a slight reddening from a bruise may be passed for food."*

- 9 CFR 381.90 – States that *"carcasses of poultry showing evidence of having died from causes other than slaughter shall be condemned."*

- 9 CFR 381.91 – 381.91(a) states *"that carcasses of poultry contaminated by volatile oils, paints, poisons, gasses, scald vat water in the air sac system, or other substances which render the carcasses adulterated shall be condemned."* Section 381.91(b)(1) states that any carcass accidentally contaminated during slaughter with the contents of the digestive tract shall not be condemned if promptly reprocessed under the supervision of an inspector and subsequently found not to be adulterated. Contaminated surfaces that are cut shall be removed only by trimming. Contaminated inner surfaces that are not cut may be cleaned by trimming, or at an approved reprocessing station away from the main processing line may be cleaned by a method that will removed the contamination, such as vacuuming, washing, and trimming. All visible specks of contamination must be removed and if the inner surface is reprocessed by a method other than trimming alone, all surfaces of the carcasses shall be treated with chlorinated water. Section 381.91(b)(2) states the conditions under which FSIS will approve a reprocessing station.

- 9 CFR 381.92 – States that *"carcasses of poultry that have been overscalded, resulting in a cooked appearance of the flesh, shall be condemned."*

- 381.93 – Section 381.93(a) states that putrefied or stinking carcasses shall be condemned. Section 381.93(b) states that any part of a carcass which is green struck shall be condemned, and if the whole carcass is affected it shall be condemned. Section 381.93(c) states that carcasses affected by post-mortem

changes that are superficial can be passed for human food after removal and condemnation of affected parts.

- 9 CFR 381.94 – Covers contamination with microorganisms; process control verification criteria and testing; and pathogen reduction standards. You will learn more about these requirements and the procedures that you perform to verify compliance when you attend the Inspection Methods class.

- 9 CFR 381.95 – Covers the disposal of condemned poultry products.

Directives and Notices related to post-mortem inspection

The Directives that cover the procedures for post mortem inspection are found in the 6000 series. Following are some examples of these directives.

- FSIS Directive 6100.1, Rev. 1 Post-mortem Livestock Inspection
- FSIS Directive 6100.3, Ante-mortem and Post-mortem Poultry Inspection
- FSIS Directive 6120.1, Finished Product Standards Program for the New Line Speed Inspection System and the Streamlined Inspection System
- FSIS Directive 6170.1, Ratite Ante-mortem and Post-mortem Inspection
- FSIS Directive 6210.2, Inspection of Poultry Feet that are Presented as Eligible to Receive the Grant of Inspection
- FSIS Directive 6240.1, Inspection, Sampling, and Disposition of Animals for Tuberculosis
- FSIS Directive 6500.1, New Poultry Inspection System: Post-Mortem Inspection and Verification of Ready-To-Cook Requirement
- FSIS Directive 7320.1, Rev. 1, Prevention and Control of Trichinella in Pork Products
- FSIS Notice 17-16, Verification of Carcasses that an Establishment Further Processes Without an Official Inspection Legend
- FSIS Notice 67-14 Unsplit Sternum of Livestock Carcasses in Slaughter Establishments
- FSIS Notice 48-14 Pathology Sample Reports Delivered Only Electronically

The regulations and directives provide the instructions for performing inspection procedures, making regulatory determinations, documenting noncompliance when appropriate, and taking regulatory actions.

ESTABLISHMENT RESPONSIBILITIES

The primary responsibility of the establishment is to ensure that its production processes result in the safe and wholesome product. In addition, FSIS regulations outline some responsibilities of the establishment that are specifically related to post-mortem inspection. There are two of these responsibilities:

- sanitary practices in preparing the carcass for post-mortem inspection,
- presenting carcasses and parts for inspection in a specified manner (called presentation), and

- facility requirements at the inspection stations

In general, the establishment's procedures to prepare livestock or poultry for inspection must take place in sanitary conditions and must use sanitary procedures to prevent contamination of the carcasses and parts (9 CFR 310.18, 381.91, and 416). For example, during livestock slaughter, the establishment must use sanitary dressing procedures to remove and skin the head, dehide or dehair and eviscerate the carcass, wash the head and carcass, and split and trim the carcass. In poultry slaughter, the establishment must use sanitary procedures to removing feathers and feet, open the carcasses, eviscerate, and shackle the carcasses.

The establishment must also ensure that the carcasses are presented for inspection in a specified manner (307, 381.76). For example, they must be hung on the line in a specified manner and spaced appropriately. The organs of livestock must be displayed in a specified order so that the inspector does not have to spend time locating them before he or she performs inspection procedures. Proper presentation helps to ensure consistent and accurate inspection. There are variations in the ways in which an establishment will present carcasses and parts for inspection. You will learn about these during the in-plant portion of your training.

The establishment is also responsible for providing appropriate inspection stations that meet regulatory requirements (307.2, 381.76). The requirements vary depending on the type of equipment used at the establishment. For example, in large livestock slaughter establishments, there may be separate inspection stations for heads, viscera, and carcasses. In large poultry slaughter establishments, there may be separate inspection stations for carcasses and for carcasses that are salvaged and reprocessed. However, if you are assigned to a very small establishment, inspection for all of the regulatory requirements may take place in one location. Regardless of the number or placement of the inspection stations, the following conditions must be provided by the establishment.

- Adequate space for conducting inspection (e.g., the size and height of the on line inspection station) (307.2(m)(1), 381.36)
- Adequate lighting for conducting inspection (307.2(b), 307.2(m)(2), 381.36)
- Hand rinsing facilities to ensure that sanitary conditions are maintained (307.2(m)(3), 381.36(c)(1)(viii))
- Condemned containers for disposal of condemned carcasses or parts (307.2(e), 381.36)

These requirements are necessary to ensure that there are adequate provisions to allow for inspection duties to be conducted appropriately.

POST-MORTEM INSPECTION PROCESS

Overview

During this section of the training, we will cover the post-mortem inspection procedures. Just as was true in ante-mortem inspection, there are three possible outcomes of the inspection.

1. passed, and thus eligible to receive the marks of inspection (310.8, 381.79);

2. U. S. Suspect, which must be retained for veterinary disposition (310.3, 381.77); and
3. U. S. Condemned, which is not eligible to receive the marks of inspection and cannot enter commerce (310.5, 381.78)

As the public health veterinarian, you may be responsible for making dispositions on carcasses and parts that are suspect. We will introduce the diseases and conditions in this module, but we will cover the specific details of veterinary disposition in another module, "Multi Species Disposition." It is during this step that the final determination is made whether to pass or condemn the carcass and parts. The primary guiding principle is whether the carcass, organ, or part is adulterated, or whether it is wholesome and fit for human food.

Sanitation

You and all other inspection personnel must always maintain proper employee hygiene when conducting inspection procedures. In most cases, the establishment will have a set of requirements, such as standard operating procedures, that are required for establishment employees. These are required by 9 CFR 416.5. For example, they may include requirements for employee hygiene such as hand washing, hair and beard nets, and using foot washes when moving between edible and inedible areas of the establishment. You must meet or exceed those standards. In addition, off line inspectors are responsible for verifying that the establishment is preparing the carcass and parts in a sanitary manner. This includes ensuring that the equipment, utensils, or any other such item used in preparing the carcass and parts are sanitary, and that the conditions in the establishment are sanitary. The establishment is required to have and to follow a set of procedures to maintain sanitary operations. We will cover the regulatory requirements and how they are verified for employee hygiene and sanitary operating procedures later when we cover the Sanitation Performance Standards and the Sanitation Standard Operating Procedures (Sanitation SOPs) that are in 9 CFR 416.

Safety

You must maintain safety with regard to the use tools, such as hooks and knives, which are used as part of the inspection process. You will learn the appropriate techniques to maintain safety, such as knife sharpening techniques and how to use hooks, during your in-plant training. There is also a separate module on in-plant safety practices.

General methods of post-mortem inspection

The general methods you will use to detect diseases, abnormalities, and contamination will involve your senses. These include:

- Sight – observing a disease lesion (abscess, tumor).
- Feel – palpating (feeling an abnormal lump in tissues, feeling abnormal firmness in an organ).
- Smell – smelling the urine odor of uremia, smelling the contents of a broken abscess).
- Hearing – listening to a carcass fall off the line on to the floor.

The purpose of post-mortem inspection is to make a decision about the wholesomeness of each poultry carcass inspected. One of the following outcomes will result from post-mortem inspection.

- If the carcass is wholesome and normal without any localized disease condition, it is passed and allowed to continue down the line.
- If the carcass is wholesome except for a localized disease condition, it is retained. It is typically routed to an area where it can be trimmed so that the unwholesome or diseased portions are removed. These removed materials are considered to be inedible and are condemned. The remainder of the carcass which is now wholesome or free of disease is allowed to continue after removal of the affected areas to become passed product.
- If the carcass exhibits abnormal signs or conditions that indicate it is unwholesome or diseased, the entire carcass is condemned.

The final consideration for carcass disposition is questionable carcasses that require further examination. Borderline or questionable carcasses are retained for veterinary disposition (livestock) or placed on the hang back or retain rack pending further review (poultry). When the inspector is undecided about the proper disposition of a carcass, the carcass is tagged and railed out or the establishment helper is notified to place the carcass on the hang back or retain rack. The public health veterinarian reviews all such carcasses and makes a final disposition of whether to pass, trim, or condemn the carcass.

<u>The importance of lymph nodes in livestock post-mortem inspection</u>

In order to detect diseases and contamination, you have to direct your attention to an area where they are likely to be observed. Diseases, abnormalities, and contamination can occur at any place on the carcass or its parts. However, diseases and abnormalities are mostly likely to produce visible or palpable lesions in specific locations. Of primary importance in organoleptic detection of disease is the lymphatic system. The lymphatics consist of vessels throughout all tissues which lead to lymph nodes. Lymph nodes range in size from just visible to 3 to 4 inches across. Their appearance has been variously described as “egg shaped” to “cigar shaped” to “spherical.” All these shapes can be normal. The consistency (firmness) is between that of warm fat and muscle. The color ranges from grey-brown to fat-colored. Some have light and dark markings. The normal range of appearances is wide, depending on the age of the animal, breed, species, and location in the body. The best way to learn what is “normal” is to look at all the lymph nodes you can under the direction of your mentor who will explain what you see.

Lymph notes function as filters for disease microorganisms and abnormal or toxic chemicals in the tissue fluids of the body. An example you may have seen is “blood poisoning” in a hand or finger of a person. Red streaks that are not blood vessels become visible up the arm and a lump, with swelling and pain, develops in the armpit. The red streaks are inflamed lymph vessels. These are normally invisible to the eye. The lump is formed by the inflamed proper axillary lymph nodes. Under the skin you can see the redness and enlargement of the nodes. When diseased organisms or toxins begin to spread around the body, the lymph nodes are among the first tissues to become visibly affected. This is the inspector’s signal that something is wrong.

The major lymph nodes are located in specific places and the fluids draining through their filter mechanism comes from specific areas of the body. The veterinarian examines the carcasses and parts retained by the inspectors. The lymph nodes and tissue responses found during these detailed examinations indicate the location and severity of the condition, and whether or not the disease has begun to spread around the animal's body. By evaluating these and the ante mortem findings, plus laboratory results if necessary, the veterinarian determines the acceptability of the carcass and parts for human food.

Some lymph nodes and tissues need to be incised so that the internal portions can be observed. The incision technique is critical. First, the cut edges must be smooth, not ragged or torn. Otherwise, the lesions of certain important diseases are difficult to detect. Lymph nodes should be sliced in thin parallel slices to expose the body of the node. Tuberculosis lesions, some abscesses, and other conditions are exposed by incision of lymph nodes. The wrist rolling motion that you will learn from your mentor permits you to observe both sides of the slice.

Livestock post-mortem inspection

The post-mortem inspection process for livestock involves the following steps:

- head inspection,
- viscera inspection, and
- carcass inspection

No step in the inspection process may be omitted.

In large establishments, inspectors are assigned to cover one of these areas and rotate to different sites according to a rotation pattern. At small or very small establishments, the inspector may perform all of the post-mortem inspection procedures on each animal. The inspection routines differ for each inspection site in each species. The differences reflect variations in anatomy, diseases, and method of dressing that the establishment uses.

In general, when abnormalities are observed while performing inspection, the following actions must take place:

1. If the disease or condition of the head, organ, or carcass is localized, have the establishment trim the affected tissues.
2. If the disease or condition is generalized and affects the majority of the head, organ, or carcass retain it for veterinary disposition.

The specific details for the inspection procedures for each of the livestock species covered by the regulations – cattle, sheep, and swine, equine – differ. However, there are similarities. We will walk through the general steps involved in swine post-mortem inspection as an example of post mortem inspection procedures. The post-mortem inspection procedures for other species are shown in the Appendix of this module. You will learn more about making veterinary dispositions when we cover the module Multi Species Dispositions.

In order to perform inspection procedures appropriately, you must be familiar with the anatomy of a livestock carcass and its parts. For example, for swine post mortem, the example we will be using, you will need to learn how to locate and identify the mandibular lymph nodes in the head; the mesenteric, hepatic, and tracheobrochial lymph nodes in the viscera; the lungs, heart, and the liver; and the kidneys of a carcass. The Appendix provides schematics outlining livestock anatomy.

Example: Swine head inspection

The head inspection procedures for swine are as follows:

1. Observe head and cut surfaces – the eyes, fat, cheek muscles, and other tissues for abnormalities.
2. Incise and observe the right and left mandibular lymph nodes – examine the closest tissues first.
3. When abnormal conditions are observed, retain the head for veterinary disposition.

Your veterinary mentor will show you how to perform these procedures in detail.

Here are some common abnormal conditions observed during head inspection.

- 311.2 - Tuberculosis may be detected during head inspection in varying degrees. The inspector must condemn the head if any amount of tuberculosis is found in the head during head inspection. The head is usually stamped at the viscera inspection station and the nodes in the jowls removed and condemned as required. Ensure that the carcass is also identified with a retain tag.

- Abscesses are another common finding during the inspection of the head. When slight, small, well-encapsulated abscesses are found on head inspection, the carcass should be tagged. When well-marked or extensive abscesses are seen, the carcass should be tagged by the head inspector. Ultimately, the disposition of the extensive or well-marked abscessed head will be condemnation (probably at the viscera inspection station) and the affected areas in the jowl will be removed and condemned.

- At the head inspection station you may see atrophic rhinitis. Swine with atrophic rhinitis may have a characteristic nose disfiguration, absence of nasal turbinate bones, and small amounts of pus or exudate in the nasal sinuses. The turbinate soft tissues may be present, but they are folded against the nasal cavity wall since the supporting bony structure has disappeared. Since this condition is usually localized, head tissues can be removed without contamination and saved for food.

In addition to observing abnormal conditions in heads, post-mortem inspectors also identify improper presentation by the establishment. Here are some examples of improper presentation of swine for inspection:

- Head missing — the head can't be inspected if it is missing. Remember, you must be able to determine at all times which parts belong to a carcass (310.23).

Therefore, the establishment must have a method of identifying the carcass and all its parts (e.g., tag).

- Mandibular lymph nodes left in the neck instead of on the head.
- Hog rings — these should have been removed as part of the cleaning operation prior to head inspection.
- Ear tags and rosin contamination.

Based on the severity and the frequency of the improper presentation, certain actions should be taken by inspection.

1. First, direct the designated establishment personnel to immediately remove the condition of improper presentation and delay inspection procedures until the condition is removed.
2. If action in #1 does not result in proper presentation, direct the designated establishment employee to stop the line and remove the condition if it cannot be removed prior to the carcass leaving the inspection area.
3. If conditions exist to the extent that the line has to be stopped repeatedly, delay inspection and ask establishment management to correct the problem.
4. The IIC may require the establishment to reduce the line speed until the conditions are favorable.

Note: Examples for head inspection of different species (e.g., cattle) are shown in the Appendix.

Example: Swine viscera inspection

Viscera include the contents (organs) of the animal's abdominal cavity. You must be able to determine at all times which parts belong to a carcass. Therefore, the establishment must have a method of identifying the carcass and all its parts (e.g., tag).

Viscera inspection includes the following steps:

1. Observe the eviscerated carcass, viscera, and parietal l (top) surface of spleen.
2. Observe and palpate mesenteric lymph nodes.
3. Palpate portal lymph nodes.
4. Observe dorsal (curved) surface of lungs.
5. Palpate bronchial lymph nodes – right and left.
6. Observe mediastinal lymph nodes.
7. Turn lungs over and observe ventral (flat) surfaces.
8. Observe heart.
9. Observe dorsal (curved) surface of liver.
10. Turn the liver over and observe ventral (flat) surface.

Your veterinary mentor will show you how to perform these procedures in detail.

When abnormal conditions are observed, retain the viscera for veterinary disposition.

Here are common abnormal conditions that are observed during viscera inspection.

- 311.7 - Arthritis--joints with localized arthritis and corresponding lymph nodes shall be removed and condemned during dressing operations and before inspection is completed.

- 311.16(a)(1) - Pleuritis--localized, chronic pleuritis with adhesions may be "peeled out" with the remainder of the carcass passed for food. If pleuritis is acute, extensive, or other associated pathology is present, the carcass and its parts should be retained for veterinary examination.

- 311.16(a)(1) - Pneumonia--lungs that have been contaminated with scald vat water resemble lungs with pneumonia

- 311.16(a)(7) - Nephritis--one or both kidneys may be affected. Localized conditions require the affected kidney(s) to be removed and condemned. If there is doubt as to whether the condition is localized to the kidney or if other pathology exists, the carcass should be retained.

- 311.16(a)(7) - Embryonal nephroma--these are tumors of the kidney. Generally, they are benign and occur more commonly in young animals. These should be retained for veterinary disposition.

- 311. 16(a)(7) - Hydronephrosis--one of both kidneys literally become a "bag of water". Normal kidney tissue is replaced by fluid. There is generally no effect upon the carcass. Affected kidneys are removed and condemned.

- 311.20 - Sexual odor--each boar hog that is slaughtered should be screened for the pungent sexual odor that is characteristic in some boar hogs. If sexual odor is detected by the viscera inspector, the carcass and viscera should be retained for veterinary disposition.

- 311.16(a) - Pericarditis--if acute, extensive, or other pathology is detected, retain for veterinary disposition. If pericarditis is localized and chronic (adhesions of the pericardial sac to the wall of the heart), the heart and pericardium is condemned, but the carcass may be passed for food.

- 311.24 - Cysticercosis (pork measles)--a parasitic condition caused by a tapeworm cyst (Taenia solium cysticercus). Similar to beef measles, it can affect any muscle tissue in the carcass. In pork, the heart seems to be the most common site. The carcass and parts must be retained for the veterinarian to examine.

- 311.19 - Icterus--the carcass has a lemon-yellow appearance. Icterus particularly affects connective tissues (tendons, ligaments, sclera of the eye, etc.). Carcasses affected with any degree of icterus are retained for veterinary disposition.

- 311.3 - Hog cholera--identified by such findings as hemorrhagic lymph nodes and red spots on belly and legs, and possibly a "turkey egg" kidney. If abnormal hemorrhages are observed, the carcass should be retained for veterinary disposition.

- 311.17 - Septicemia--a generalized inflammatory conditions caused by pathogenic bacteria and associated toxins in the blood. Most, or all, of the body lymph nodes may be enlarged, hemorrhagic, and edematous. Kidneys may have petechiae (small pinpoint hemorrhages). Other pathology may be present. Retain the carcass for veterinary disposition.

- 311.24 - Ascarids--the larva of these roundworms frequently migrate through the liver and cause scarring on the livers surface. "Slight" scarring may be trimmed (spotting the liver). More than slight evidence of ascarids requires the liver to be condemned.

- 311.14 - Abscesses--If the carcass has been tagged by the head inspector for a slight cervical abscess and the viscera inspector finds tuberculosis (TB) in the viscera, the carcass and viscera must be retained for veterinary disposition. If no lesions are found in the viscera, the viscera inspector will permit the head to be used for food after complete removal and condemnation of the mandibular and adjacent lymph nodes in the jowls. However, if the establishment does not choose to trim as described, the head and jowls will be condemned.

- 311.12 - Tuberculosis (TB)--the primary seats of TB are defined as the mandibular, the mesenteric, and the mediastinal lymph nodes in swine. These sites are regarded as the primary seats for disposition purposes only and do not necessarily have any correlation with the frequency at which tuberculosis is found in any location. Probably the most common sites at which tuberculosis lesions would be found would be the mandibular and mesenteric nodes and the liver. The food inspector is authorized to make a limited disposition for tuberculosis on a swine carcass with TB lesions in only one primary seat. For example, if tuberculosis is found in the mesenteric lymph nodes only, it is not necessary to tag the carcass and retain it. However, if there is TB in more than one primary seat or in any site other than a primary seat, then that carcass and viscera must be retained for veterinary disposition.

- 311.30 – Suffocation (Asphyxia) - a scarlet red appearance of the carcass and organs that are engorged with blood; must be retained for veterinary disposition.

As in head inspection, there are various forms of improper presentation that occur at the viscera inspection station. Contamination with feces or ingesta is one of the most common defects. Hair, toenails, pus, bile, and parts of viscera missing are other common examples of improper presentation. When improper presentation occurs, take the same actions as when it occurs at head inspection, which includes the following.

1. First, direct the designated establishment personnel to immediately remove the condition of improper presentation and delay inspection procedures until the condition is removed.
2. If action in #1 does not result in proper presentation, direct the designated establishment employee to stop the line and remove the condition if it cannot be removed prior to the carcass leaving the inspection area.
3. If conditions exist to the extent that the line has to be stopped repeatedly, delay inspection and ask establishment management to correct the problem.
4. The IIC may require the establishment to reduce the line speed until the conditions are favorable.

Note: Examples for viscera inspection of different species (e.g., cattle) are shown in the Appendix.

Example: Swine carcass inspection

There are four steps to carcass inspection.

1. Observe the back of the carcass. This may involve observing it in a mirror, or turning the carcass manually
2. Observe the front parts and the inside of the carcass.
    a. Observe all cut surfaces.
    b. Observe all body cavities (pelvic, abdominal, and thoracic).
    c. Observe the lumbar region.
    d. Observe the neck region.

3. Grasp, turn, and observe the kidneys (both sides).

Your veterinary mentor will show you how to perform these procedures in detail.

If abnormal conditions seen on carcass inspection do not require veterinary disposition, the inspector can have the establishment employee properly trim the carcass. However, some abnormal conditions require retention for veterinary disposition. Here are some examples of abnormal conditions that may be seen during carcass inspection.

- 311.7 - Arthritis--arthritis in a joint may be indicated by the appearance of the lymph nodes associated with that joint

- 311.14 - Abscesses--abscesses may be found anywhere in the carcass or its parts.

- 311.6 - Diamond skin disease--these carcasses should be retained for veterinary disposition.

- 311.16(a)(7) - Nephritis

- 311.24 - Cysticercosis--cysticercosis (measles), or cysts, can be found in any muscle tissue. Retain for veterinary disposition.

- 311.13 - Melanoma--these are tumors that contain black pigment (melanin). Retain these for veterinary disposition.

- 311.11 - Neoplasm (malignant lymphoma)--these tumors are commonly found in and around lymph nodes, but may be detected anywhere. Anytime you detect an abnormal mass (tumor), you should retain the carcass for veterinary disposition.

- 311.16(a)(7) - Cystic kidney--clear, fluid filled cysts of varying sizes. Condemn the kidneys (unless the condition is slight) and pass the carcass for food.

- 311.16(a)(7) - Embryonal nephroma--retain for veterinary disposition.

- 311.24 - Kidney worms--this condition can also be seen in the soft tissue of the carcass and abdominal viscera.

- Adhesions--these fibrous bands form as a chronic response to inflammation and are an attempt by the body to heal. Condemn affected parts and pass the carcass if no other pathology is noted.

- 311.14 - Abscess in the backbone--always check carefully along the backbone of the split carcass. It is possible to see abscesses, neoplasms (tumors), or evidence of trauma (fractures and bruising).

- 311.14 - Bruises--bruised tissue should be trimmed and condemned. If evidence of infection exists, retain the carcass for veterinary disposition.

- 311.2 - Cervical tuberculosis – retain the carcass for veterinary disposition.

- 311.14 - Slight cervical abscess, or well-marked or extensive abscess – retain the carcass for veterinary disposition.

- 311.30 – Suffocation (Asphyxia) - a scarlet red appearance of the carcass and organs that are engorged with blood; must be retained for veterinary disposition.

- 310.18(a) - Contamination (Overscald) – carcasses that have been overscalded will have a cooked appearance and will usually have varying degrees of mutilation and contamination of tissues with scald vat water.

Once again, when improper presentation occurs, take the same actions as when it occurs at head or viscera inspection, which includes the following.

1. First, direct the designated establishment personnel to immediately remove the condition of improper presentation and delay inspection procedures until the condition is removed.
2. If action in #1 does not result in proper presentation, direct the designated establishment employee to stop the line and remove the condition if it cannot be removed prior to the carcass leaving the inspection area.
3. If conditions exist to the extent that the line has to be stopped repeatedly, delay inspection and ask establishment management to correct the problem.
4. The IIC may require the establishment to reduce the line speed until the conditions are favorable.

Note: Examples for carcass inspection of different species (e.g., cattle) are shown in the Appendix.

<u>Poultry post-mortem inspection</u>

Post-mortem inspection for poultry focuses on each carcass, its organs, and parts. The specifics of the procedures will vary depending on which of the six inspection systems – traditional, SIS, NELS, NTIS, NPIS, or Ratite – is being used at the establishment. You will learn the specifics of the inspection procedures in-plant with your mentor. However, following is a general overview of the procedures that must be performed. If you are working at a very small or a small establishment, you may perform all of the inspection

procedures yourself. If you work at a large establishment, there will be inspection stations where different inspection procedures are performed.

The conditions are listed on FSIS Form 6000-16 (Lot Tally Sheet), and the criteria for condemnation in each category is as follows.

FSIS Directive 6100.3 covers post-mortem disposition of poultry products.

Let's review the disease conditions and inspection determinations that you must make.

- 381.81 – Tuberculosis One definitive lesion is all that is required to condemn a poultry carcass for tuberculosis.

- 381.82 – Leukosis This category includes several neoplastic diseases caused by various viruses. All produce tumors in domestic poultry and present similar gross lesions. One definitive lesion justifies condemnation of the carcass.

- 381.83 - Septicemia/toxemia The Agency considers both conditions under the general category of septicemia/toxemia, commonly referred to as sep/tox. If a carcass shows systemic change, it is condemned for sep/tox.

- 381.86 – Synovitis/Tendonitis Synovitis is caused by a number of organisms, most often members of the genus *Mycoplasma*. Injury and nutritional deficiencies also lead to synovitis. A carcass with synovitis is not condemned *unless* it also shows systemic or sep/tox changes.

- 381.87 – Tumors This category refers to tumors other than those of the leukosis complex and keratoacanthomas. Some of the more common tumors include squamous cell carcinomas, adenocarcinomas, leiomyomas, and fibromas. Condemn a carcass for tumors if there is gross evidence of metastasis.

- 381.89 – Bruises If bruises cause systemic change in a carcass, or if there is *no* part of the carcass that can be salvaged, the carcass is condemned and recorded under this category. Otherwise, if *any* part *can* be salvaged from the carcass, the bruises are trimmed and the remainder of the carcass is passed.

- 381.90 – Cadaver Poultry that die from causes other than slaughter are condemned under the cadaver category.

- 381.91 – Contamination This category is for carcasses that are so contaminated they cannot be inspected or made wholesome by reprocessing.

- 381.92 – Overscald The muscle must be cooked through the level of the *deep pectoral* muscle in order to be classified as an overscald.

- 381.84 – Airsacculitis Numerous microorganisms cause airsacculitis, which is inflammation o*f air sacs*. Carcasses are condemned if airsacculitis is extensive, or if carcass exhibits airsacculitis along with systemic changes.

- 381.86 Inflammatory Process (IP) - When the condition is generalized, condemn the carcass.

- 381.88 Parasites - Organs or parts of carcasses found to be infested with parasites shall be condemned. If the entire carcass is affected, the bird will be condemned.

Veterinary supervisors may check the accuracy of inspector dispositions by observing birds upstream or downstream from the inspector or by checking birds and parts in the condemn barrel.

Salvage of Carcasses Away From the Post-mortem Inspection Station (381.76)

The term salvage refers to the actions the establishment takes to trim away any unwholesome or diseased portion of a carcass that is localized (381.76). The establishment is not required to have a written procedure for each type of salvage; however the procedure must be verifiable. The procedures must be conducted under sanitary conditions, with adequate facilities, and personnel must be available to conduct the procedures. There should be a continuous product flow without pileup or delay.

Facilities at salvage stations should include:

- adequate space located in the eviscerating area
- a retain rack designed to prevent cross-contamination
- a trough or table sloped and properly drained
- a singer, if there is not one in the picking room
- containers for chilling the product
- a spray nozzle with proper fittings to clean carcasses
- a facility for washing hands, tools, etc., such as a gooseneck

Contamination Knife Salvage

When a carcass is designated for knife salvage because of body cavity contamination, most establishments follow a salvage technique similar to the following:

- remove the viscera
- hang the carcass in a designated area on the retain rack
- transfer the carcass to the salvage station and hang in such a way as to distinguish it from a salvageable airsacculitis carcass (This varies by establishment. Some establishments choose to hang some types of salvage birds by the neck, whereas others have a specific mark that is placed on the carcass to designate the type of salvage procedure)
- wash external carcass surfaces thoroughly before any cutting
- properly trim the carcass without cutting into the body cavity or opening cut surfaces
- usually save both wings, both legs, and the breast muscle, including the deep and superficial pectoral muscles

All knife salvage must be done in a sanitary manner and must not produce contaminated or adulterated product.

Airsacculitis Knife Salvage

Special attention must be given to salvaging carcasses with airsacculitis because of the complexity of the interclavicular air sac and the associated diverticuli. If the visible part of the interclavicular air sac is inflamed, assume all of it is inflamed and salvage the carcass accordingly. All exudates must be removed. The kidneys must be removed if renal pathology is present or airsacculitis is present specifically in the abdominal air sac membranes making the kidneys an affected tissue, and the posterior part of the carcass is salvaged for airsaccultitis per 9 CFR 381.84. The viscera must be condemned.
Note: Hepatic or splenic pathology which is determined by IPP to be localized and visibly limited to the affected organ require only the affected visceral organ to be condemned. Localized pathology of the liver or spleen does not require simultaneous condemnation of the kidneys unless the kidneys are also affected by visible pathological changes.

When a carcass is designated for knife salvage because of airsacculitis, most establishments follow a salvage technique similar to the following:

- The salvaged carcass with airsacculitis is usually marked and hung in such a way as to distinguish it from a salvageable contaminated carcass.
- Other steps, such as removing the viscera, transferring the carcass to the salvage station, etc. are also followed for carcasses with airsacculitis.
- The following portions of the carcasses are usually salvageable: the wings (minus the portion containing the humeral bones), the legs, and the breast muscle. The area of the breast muscle around the first wing joint is condemned and the deep pectoral muscle anterior to breastbone bursa is condemned. All the rest is eligible for salvage.

All knife salvage must be done in a sanitary manner and must not produce contaminated or adulterated product.

Airsacculitis Salvage

When the interclavicular air sacs are not involved in airsacculitis, knife salvage is not required. The requirement for this type of salvage is removal of all exudates and the kidneys if renal pathology is present or airsacculitis is present specifically in the abdominal air sac memebranes making the kidneys an affected tissue, and the posterior part of the carcass is salvaged for airsaccultitis per 9 CFR 381.84. This can be accomplished by vacuuming the carcass with a vacuuming device, or by removing all exudates and kidneys by hand. This type of salvage is appropriate when there is involvement of the abdominal and/or thoracic air sacs without involvement of the interclavicular air sacs, because the thoracic and abdominal air sacs do not have diverticuli that extend into bone.

Reprocessing of Carcasses due to Contamination

Contamination Reprocessing

Carcasses that have their body cavities contaminated with digestive tract contents may be rendered unadulterated by prompt washing, trimming, and/or vacuuming instead of knife salvage. The procedure for removing digestive tract content is called reprocessing.

381.91(b)(1) Online Reprocessing: Poultry accidentally contaminated with digestive tract contents may be cleaned by applying an online reprocessing antimicrobial intervention to all carcasses while remaining on the line in their individual shackle. If antimicrobial agents are applied to carcasses or parts prior to entering the chiller, parameters of their use are subject to FSIS approval. Establishments must incorporate procedures for the use of any online reprocessing intervention system into their HACCP plans, SSOPs or other prerequisite programs.

Establishments may also elect to utilize offline reprocessing, 381.91(b)(2), where carcasses are removed from the line due to contamination and directed to another station for a combination of trimming and antimicrobial treatments. Offline reprocessing must have adequate facilities, trained personnel, and the procedure must be accomplished in a sanitary manner while maintaining product flow.

Facilities typically seen at the offline reprocessing station are:

- adequate space in the eviscerating room or a suitable adjacent area
- a retain rack designed to prevent cross-contamination
- a trough or table that is sloped and properly drained
- containers for chilling product
- a knife rack or stand
- conveniently located hand-washing facilities
- spray nozzle with proper fitting for cleaning carcasses
- water containing 20-50 ppm available chlorine, or another approved antimicrobial substance for rinsing all reprocessed carcasses (CFR 381.91(b)(2))

When a carcass is designated for reprocessing because of body-cavity (inner surface) contamination, the establishment is required to:

- remove the viscera and hang the carcass in a designated area on the retain rack
- transfer the carcass to the reprocessing station and suspend it to prevent contamination during reprocessing
- remove the crop
- wash the external surface thoroughly
- remove contaminants by trimming, vacuuming, and/or washing. Any contamination of cut surfaces must be removed by trimming
- thoroughly rinse with water containing at least 20 ppm available chlorine (CFR 381.91(b)(1)), or other approved antimicrobial treatment
- measure and record the chlorine concentration at least once a day
- monitor reprocessed birds
- make birds available for reinspection by the FSIS inspector

If retain racks at the USDA inspection station or reprocessing station are filled, the IIC should allow the establishments the option of disposing of contaminated carcasses or adjusting the production rate. Carcasses disposed of by the establishment because of reprocessing pile ups should be recorded as “Plant Rejects”, because the establishment is choosing not to reprocess those carcasses.

RESTRICTED PRODUCTS

The livestock slaughter regulations outline requirements related to restricted products (315). A restricted product is defined as any meat or meat food product that has been inspected and passed but cannot be released for human consumption until it has been subjected to a required treatment because it has a disease or condition that might be transmitted to humans if the meat is not treated. There are four types of restricted product treatments. They are:

- Refrigeration (311.23(a)(2))
- Heating (311.23(a)(2))
- Cooking (311.2(d)(f)(g), 311.18(e), 311.24, 311.25)
- Use in comminuted cooked meat food product (311.20(b), 311.35(c), 311.37)

Restricted product will be used for human food after required treatments are complete. For this reason, condemned and inedible products are not examples of restricted product.

The establishment must maintain control over all restricted product. FSIS inspection personnel must verify that the establishment has met the conditions associated with the restrictions before this type of product is allowed to be used as human food. Failure to adequately control certain products may result in the transfer of disease or pathogen from the product to the consumer.

Control of any restricted product begins at the time the veterinarian makes a disposition. First, a decision is made to pass the carcass with a restriction. A thorough check is made to see that all visible lesions are removed from the carcass (311.23). Then, the carcass is retained. If any additional lesions are discovered at a later time (while the carcass is being boned for example), the veterinarian will make a new disposition based on the new findings.

Some establishments have adequate facilities for treating restricted product (e.g., cooking, freezing). For establishments that do not have such facilities, the establishment is allowed by regulation to ship restricted product to another official establishment that has the needed facilities (316.18). To maintain security, the restricted product must be shipped under official government (FSIS) seal.

In certain cases, establishments may elect to bone a restricted carcass prior to the carcass undergoing a specified treatment. For example, the establishment manager may request that, in order to bone a carcass with beef measles passed with a freezing restriction, the establishment be allowed to remove it from the retain cage. An inspector must release the carcass from the retain cage and accompany the establishment employee as he/she takes the carcass to the boning area. Once the carcass is in the boning area, it must be boned in a manner that prevents it from being intermingled with non-restricted product. If the restricted product is to be boned out prior to regular boning operations, all restricted product must be removed and the entire boning area must be thoroughly cleaned before regular boning commences. This must include employee equipment such as knives, hooks, and scabbards used while boning restricted product. To avoid a complete cleaning of the boning area, the establishment may elect to bone the restricted product after regular boning operations are completed. This is acceptable, however, all non-restricted product must be prevented from contacting, or becoming

intermingled with non-restricted product. Anytime restricted product is being handled, it must be under the direct control of inspection. For boning, this means under direct visual surveillance, or secured in a locked or sealed boning room.

Records must be kept on boneless restricted product, as well as other restricted product. The records should be kept on file in the government office. The records should contain the following information:

1. U.S. Retain tag numbers(s).
2. Quantity of restricted product (e.g., number of carcasses, pounds boned, or pounds boxed).
3. Quantity of condemned material (i.e., trimmed visible lesions).
4. Destination of product (if shipped under seal).
5. Inspector's name
6. Date

Let's review each of the four categories involving restricted product.

Passed for refrigeration

Only carcasses that are moderately affected with beef cysticercosis (beef measles) may be passed with a refrigeration restriction (311.23(a)(2)). This actually means the carcass or boned meat must be frozen. Freezing this product destroys any tapeworm cysts that were not identified and removed during inspection.

The regulations list separate and specific time/temperature treatment requirements for carcasses and boxed boned meat affected with beef measles that have been designated "Passed for Refrigeration" by the veterinarian. The carcass may be branded with a "U.S. Inspected and Passed" brand prior to placing it in the freezer because it is very difficult to apply a legible brand to a frozen carcass. After a successful 10-day treatment period, the establishment is then free to ship the carcass. Carcasses may be boned under control prior to freezing. During boning, the establishment is permitted to place the boned meat from restricted carcasses directly into boxes bearing the mark of inspection. The boxes can then be retained in the freezer for the 20-day period. The establishment is allowed to do this to avoid considerable unnecessary work in transferring unmarked frozen meat to boxes bearing the mark of inspection.

Passed for heating

There are two conditions that may be "Passed for Heating" by the veterinarian. One is cysticercosis of sheep (sheep measles), the other cysticercosis of beef (beef measles) (311.23(a)(2)). Notice that beef measles may be passed for refrigeration or passed for heating. A cattle or sheep carcass, or meat derived from such carcasses passed with a heating restriction, must be heated throughout to a minimum internal temperature of 140°F.

Passed for cooking

Carcasses with the following diseases or conditions may be "Passed for Cooking."

- Tuberculosis – 311.2

- Caseous lymphadenitis – 311.18(e)
- Swine cysticercosis (pork measles) – 311.24
- Carcasses with parasites not transmissible to humans – 311.25

Carcasses passed for cooking must reach a minimum temperature of 170°F for not less than 30 minutes. These carcasses are marked with a "US Passed for Cooking" stamp by the veterinarian when he or she makes this disposition.

Rendering the restricted carcass and parts into lard, pork fat, or tallow will accomplish the 170°F for 30 minutes requirement. The cooking and rendering of restricted product must be performed under the control of inspection. Once the restricted product is placed into the rendering tank, the tank must be secured with an official government lock or seal to maintain control and prevent removal of its contents. The inspector removes the seal and releases the product after the time/temperature requirements have been met.

Passed for use in comminuted cooked product

The fourth group of restricted product consists of those carcasses passed for use in comminuted cooked product. There is a difference between this restricted product category and "Passed for Cooking." Passed for cooking requires subjecting the product to 170°F for not less than 30 minutes. There is not such a time/temperature requirement with product passed for comminuted cooked product. The only restriction imposed on these products is that they be used only in comminuted cooked products. Comminuted cooked food products are those that are finely ground and have a uniform appearance, such as frankfurters and bologna. These products are normally cooked at a temperature near 160°F.

There are two conditions for which carcasses may be passed for use in comminuted cooked product by the veterinarian. The first is certain carcasses affected with eosinophilic myositis (EM) (311.35(c)). The establishment may ship these carcasses prior to meeting the required restrictions. As with control of other restricted product, carcasses with EM passed for use in comminuted cooked product must be shipped under official seal.

The other product in this restricted category is boar carcasses with less than pronounced sexual odor (311.20(b), 311.37). As in the case with all restricted product, inspection must have positive control over these carcasses. A retain tag is used to identify carcasses passed for use in comminuted cooked product. If boar carcasses or parts with less than pronounced sexual odor are to be shipped elsewhere for boning, rendering, or use in comminuted cooked product, they must be shipped under seal like all other restricted product. However, if the boned, boxed meat from these carcasses is properly packaged and labeled "Boar Meat for Use in Comminuted Cooked Product Only," shipping under seal is not necessary. Restricted boar meat properly packaged and labeled this way is the only exception to the rule that restricted products must be shipped from one establishment to another under seal.

For review purposes, the following chart lists those conditions that the veterinarian may pass with a restriction, the regulation reference and the specific restrictions.

CONDITION	REG.	FREEZING (15°F) Days: 10-carcass 20-boxed	COOKING 170°F/ 30 min.	HEATING 140°F	COMM. COOKED PRODUCT
Beef Measles	311.23	X		X	
Sheep Measles	311.25			X	
Pork Measles	311.24		X		
Tuberculosis	311.2		X		
Caseous Lymphadenitis	311.18		X		
Parasites (not transmissible to humans)	311.25		X		
Sexual Odor Of Swine	311.20				X
Eosinophilic Myositis (EM)	311.35				X

Trichinosis

Trichinosis is a disease in humans that may be contracted from swine carcasses infested with the parasite *Trichinella spiralis*. Some pork products are treated to destroy trichinae. These pork products, however, are not considered as passed with a restriction. Trichinae control in the U.S. relies on consumer education. That is, all pork muscle products are considered potentially contaminated and must be thoroughly cooked before being eaten.

This is quite different from many European countries. They often utilize special techniques to examine carcasses for the presence of trichinae and, therefore, when product fr, om the United States is exported to these countries, an export certificate certifying that products have been treated to destroy trichinae must accompany the shipment. IPP are to follow the guidance in FSIS Directives 9000.1, Export Certification, and 9000.2, Inspection and Export Certification of Livestock Intestines or Casings when certifying product for export. Additionally, IPP should follow the guidance in FSIS Directive 7320.1, Revision 1, Prevention and Control of Trichinella in Pork Products, Chapter II-Certifying Fresh/Frozen Raw Pork Products for Export when Produced under Pork Quality Assurance Plus (PQAPlus) Programs for Trichinella Mitigation, if applicable.

On May 31, 2018, the Food Safety and Inspection Service (FSIS) published the final rule "Elimination of Trichinae Control Regulations and Consolidation of Thermally Processed, Commercially Sterile Regulations" (83 FR 25302). The final rule eliminated the prescriptive requirements in 9 CFR 318.10 for pork products to be treated to destroy

Trichinae (*Trichinella*). FSIS removed 9 CFR 318.10 because the regulations were inconsistent with the HACCP regulations (9 CFR part 417). The HACCP regulations require establishments to consider food safety hazards in their hazard analysis (including *Trichinella*). The final rule became effective July 30, 2018.

The final rule requires establishments producing RTE and NRTE pork products to determine in their hazard analysis if *Trichinella* is a hazard reasonably likely to occur (RLTO) or not reasonably likely to occur (NRLTO) based on their processes. If *Trichinella* is a hazard that is RLTO, then establishments must include control procedures for this parasite in their HACCP plans, including the critical control points (CCPs) designed to control the parasitic hazard (9 CFR 417.2(c)(2)) and the critical limits that must be met at each CCP (9 CFR 417.2(c)(3)). Establishments are also required to maintain supporting documentation to justify the decisions made in their hazard analysis (9 CFR 417.5(a)(1)).

Under HACCP, most establishments may determine that *Trichinella* is NRLTO in fresh raw pork products produced from market swine because those products are customarily well-cooked and the products bear Safe Handling Instructions (SHIs). Examples of products that are customarily well-cooked include fresh pork (i.e., raw or uncured), fresh unsmoked sausage containing pork muscle, tissue, and bacon and jowls. All of these products were previously listed in 9 CFR 318.10(a).

There are certain other less commonly produced raw and NRTE pork products that are not customarily well-cooked or that present an added risk of infection with *Trichinella.* For these other products, establishments need to prevent or control *Trichinella* through either a prerequisite program or a CCP to support decisions in their hazard analysis. These other products include:

1. Pork products that are prepared in such a manner that the product might be eaten rare or without thorough cooking because the appearance of the finished product makes it hard for the consumer to visually determine if the product has been fully cooked. Such pork products include ground meat mixtures including those containing pork and beef as well as pork and other ingredients; poultry products containing pork muscle tissue; bacon wrapped products; breaded pork; raw marinated pork in dark sauces; pork products containing ingredients such as annatto, red wine, paprika, red pepper, etc. that can alter the appearance; cured pork; and cured and smoked pork. For these raw and NRTE products, one or more processing steps make it difficult for the consumer to visually determine whether the product has been fully cooked; and

2. Feral swine that have an increased risk of infection with *Trichinella*.

FSIS has published a Compliance Guideline titled FSIS Compliance Guideline for the Prevention and Control of Trichinella and Other parasitic Hazards in Pork Products (*Trichinella* Compliance Guideline). The following Table summarizes the options recommended in that Guideline:

List of Options used to Prevent and Control *Trichinella* in Pork and Products Containing Pork	
Option 1	Acquire pork products from carcasses or carcass parts found to be free of *Trichinella* by a validated testing method
Option 2	Obtain pork products from swine producers who participate in the Trichinae Certification

	Program or another APHIS-approved validated *Trichinella* preharvest safety program
Option 3	Label NRTE pork products, including all forms of fresh pork to indicate the products require additional treatment by the consumer
Option 4	Treat NRTE pork products for the destruction of *Trichinella* that might be eaten rare or without thorough cooking because of the appearance of the finished product using (1) heating, (2) freezing, (3) curing, (4) high pressure processing (HPP), or (5) irradiation
Option 5	Develop alternative *Trichinella* control procedures not included in Option 4

Establishments may follow any of the 5 options described in the table above including the option to use special labeling (Option 3) if they produce: 1) pork products that are prepared in such a manner that the product might be eaten rare or without thorough cooking because the appearance of the finished product makes it hard for the consumer to visually determine if the product has been fully cooked ; or 2) pork products from feral swine. Establishments may choose to adopt different procedures than those outlined in the guideline, but they would need to support why or how those procedures are effective. More detailed guidance is available in FSIS Directive 7320.1, Revision 1.

As a safety factor, inspection personnel should consider all pork to be potentially contaminated with trichinae. This is why pork products must be kept separate from meat products of all other species. If pork and beef are both boned in the same establishment, a complete separation of the two products must be maintained at all times. This must either be a physical separation of the products or the two products must be worked at different times. For example, if pork is boned on a table in the morning, and beef is to be boned on the same table later in the day, a thorough cleanup of the area and all equipment must be done before the beef is processed in order to prevent cross-contamination. An alternative to this would be for the establishment to process pork at the end of the day after all other product has been removed and there is no possibility that non-pork products could come in contact with pork products. The same rule applies to grinding product. A small amount of pork tissue left in the grinder could potentially contaminate beef if there was not a thorough cleaning and sanitizing of the grinder between the two products. If pork products were ground after all other product had been ground and removed from the area, a cleanup of the grinder would not be required. One final example: Some establishments may be allowed to reuse shipping containers if the containers are in good condition. You would not allow this practice if the containers had previously been used to package pork products and the establishment wished to use them again for beef, lamb, or some other species. Always be alert for potential cross-contamination and its possible deleterious effects on public health.

ESTABLISHMENT RESPONSIBILITY FOR DEALING WITH CONDEMNED AND INEDIBLE PRODUCT

Condemned product is product that has been determined through inspection to be diseased or condition that renders it unfit for human consumption. It is prohibited from entering commerce for use as human food (314, 318.95).

Inedible product is any product that is adulterated, uninspected, or not intended for use as human food. The term inedible refers to product that by its nature is not handled as

human food (301.2). Examples include bones, uncleaned intestines, lungs, reproductive organs, feet, etc. If inedible product is diseased or has the appearance of edible product, it must be handled as condemned.

Both condemned and inedible products are not fit for human consumption. Due to the edible appearance of condemned product, its control is most crucial and the requirements found in the regulations are very specific. Edible product may have a similar appearance to condemned product and some inedible product.

Principles of control

FSIS control of condemned and inedible product involves five principles:

- -Identification
- -Custody
- -Separation
- -Destruction
- -Documentation

FSIS personnel must monitor the establishment's handling procedures of condemned and inedible product to assure that it is properly identified, maintained in custody, kept separate from edible product, and properly destroyed. Additionally, all actions taken must be appropriately documented.

Identification

As has been discussed, condemned products may look edible. For this reason they must be properly identified. The regulations require that each condemned carcass, part, or visceral organ be marked with the "U.S. Inspected and Condemned" brand (312.6(a)(5), 381.101). If the condemned product cannot be branded because of its size or texture, it must be placed in a container identified with the words "U.S. Condemned." Condemned product is to be disposed of by tanking.

An exception in the regulations allows the salvage of certain classes of condemned product for the production of pet animal food (314.11). One example is beef livers condemned for human consumption but allowed for use in pet food. The system used to identify product that is condemned versus product that is allowed for animal food must be consistent.

Custody

The FMIA requires that the inspector be able to certify that all condemned product is properly destroyed. To assure this, security of condemned product is essential. The regulations state that all condemned product must be kept in custody (security) of inspection personnel until it is destroyed for human purposes on or before the close of the day on which it was condemned. Destruction can be accomplished by incineration, rendering (tanking), or denaturing (314.1, 314.3). Custody involves direct supervision or security. This means that the condemned product must either be within sight of an inspector at all times or be placed in a secure container or room equipped with an official lock or seal. Therefore it is not permissible for inspection personnel to allow

establishment personnel to leave indentured condemned or inedible product on the kill floor during lunch or other break periods. Once condemned and inedible product is destroyed, or properly denatured, custody is no longer required.

Organs and parts (e.g., stomachs, intestines, bones, and feet) may be saved for edible (human) food at some establishments. Others may save these organs and parts as inedible product for animal food production. This is permitted provided that the establishment properly identifies the organs and parts. If the organs and parts are not used for either purpose, the product doesn't require any special security if kept separate from edible product. If it is shipped off premises for rendering, the product doesn't require denaturing as long as the establishment's handling of the product results in an inedible appearance (e.g., denaturing). Hair, hide, horns, and hooves of any animal are products considered naturally inedible. It is not necessary to require special identification or denaturing, but they must be kept separate from edible product.

Separation

Condemned and inedible products must be kept separate from edible products. A physical separation of edible and inedible facilities must be maintained to avoid cross-contamination. Contamination of edible products with materials from inedible and condemned product has potentially grave public health consequences. Inedible containers brought into edible departments must be watertight, acceptably clean, and properly identified. There are two types of inedible product containers. Containers for product condemned to tankage are marked "U.S. Inspected and Condemned." Those for product condemned for human use (inedible) but eligible for pet animal food are identified as "Inedible."

Carcasses of animals found dead or animals condemned on ante mortem inspection are not to be brought into or through an edible product area (314.8). Dead animals, except those that die en-route and are received with other livestock to be slaughtered, may not be brought onto the premises (314.7). Depending on the establishment facilities, ante mortem condemned animals may be skinned and slashed or slashed through the skin into major body muscles and the body cavities followed by the application of denaturant to all parts of the carcass. Many states, however, have regulations prohibiting the transport of opened carcasses, so an alternate method is approved. The denaturant may be injected into major muscles and cavities. This method is approved for carcasses of animals condemned on ante mortem inspection but not for carcasses condemned on postmortem inspection.

Bile historically has been regarded as inedible and when contamination of edible product occurs it must be removed before completion of inspection by FSIS personnel. There are provisions allowing that inedible bile can be saved for manufacturing uses and stored in edible product areas. Where it is allowed, bile must be segregated, handled, and labeled as an edible product.

Destruction

There are three basic methods approved for making condemned and inedible meat products incapable of being used as human food. They are:

-Rendering (314.1)
-Incineration (314.3)

-Application of approved denaturants (314.4)

Inedible rendering is a process by which materials are heated sufficiently to destroy them for human food. When the establishment has its own facilities to perform the rendering process this is termed "on-premises" rendering. Many establishments do not have such facilities. Instead, they may ship condemned and inedible materials to an outside rendering facility. This is referred to as "off-premise" rendering.

Tanking is when condemned product is placed in a rendering tank under the supervision of an inspector who would then seal the tank. Once the contents are heated adequately to destroy them for human purposes, the inspector will then remove the seal, thereby releasing it from his/her custody. This method is rarely, if ever, used today. Establishments that perform their own "on-premises" rendering today generally utilize hashers and/or pre-breakers as a pre-tanking preparation of condemned product. This gives an inedible character and appearance to the product. For this reason, custody is not necessary once the material has been hashed. In addition, there is no requirement to use denaturant on this product to be rendered on-premises. However, prior to hashing, custody of the product must be maintained. This includes all equipment prior to the hasher. For example, if an auger is used to convey condemned material to the hasher, it must be covered and sealed or be located in a secured room.

Whenever condemned materials are to be shipped to another site, they must be properly denatured. This is true whether the material has been hashed or not.

If the establishment doesn't have inedible tanking facilities and it does not send condemned product for off premises rendering, all condemned product must be destroyed (under inspector custody) by incineration or by the application of an approved denaturant. A listing of acceptable denaturing agents may be found in two sources: the Regulations and the "List of Proprietary substances and Nonfood Compounds." Before an approved denaturing agent is applied, the product must be freely slashed so that pieces are less than 4" in diameter. This allows the denaturant to contact all parts of the product. Denaturants change the color and/or odor of products sufficiently to destroy them for food purposes.

In addition to any approved denaturant compounds found in the "List of Proprietary substances and Nonfood Compounds," there are three types of denaturants approved for use on product condemned to tankage. They are:

-Crude carbolic acid
-Cresylic disinfectants
-A formula consisting of FD&C green color No. 3, oil of citronella, detergent, and water

A different group of denaturants are used on inedible product condemned for human food but salvaged for animal food. This is because the above agents would make the product unfit for even animal food. Animal food denaturants include:

-FD&C green color No. 3
-FD&C blue color No. 1
-FD&C blue color No. 2
-Powdered Charcoal
-Any compound approved for such use in the "List of Proprietary substances and Nonfood Compounds" book

Documentation

Inspection actions regarding the control of condemned products must be properly documented. On ante mortem, actions might be recorded on FSIS Form 6150-1 (Identification Tag-Antemortem) or FSIS Form 6502-1 (MP 35) (US Reject/Retain Tag). FSIS Form 6750-1 (Daily Tanking Report) is a report (used at the option of the frontline supervisor) to document the control of condemned products in slaughter establishments. All establishments that ship condemned of inedible product must have the appropriate permissions from local, state, or federal officials. The documents must be available for FSIS review.

Specimens of condemned or inedible materials for educational, research or other nonfood purposes may be released from the establishment under a permit issued by the IIC. The application is FSIS Form 6700-2 (MP 403-10) (Application and Permit to Obtain Specimens from Official Establishments). If institutions or individuals wish to obtain specimens on an ongoing basis, the permit must be renewed annually.

This form is also the permit to ship undenatured lungs for pharmaceutical or animal food use. Undenatured lungs for pharmaceutical purposes must be labeled "Inedible [Species] Lungs - For Pharmaceutical Use Only." If an establishment wishes to ship undenatured lungs for animal food, several requirements must be met. Permission must be obtained in writing from the district manager. The lungs must be shipped directly to an animal food manufacturer, zoo, mink farm, or storage warehouse. Shipping containers must be labeled "[Species Lungs - Not Intended for Human Food" and return copies of the shipping certificate must indicate to the inspector that the shipment reached its destination.

Shipment of undenatured condemned carcasses eligible for use as animal food may be approved. This requires a special permit issued by the District Manager. This product must be shipped directly to a manufacturer of inedible products. Additionally, there are special labeling and container sealing requirements.

Poultry

The regulations related to the handling and disposal of condemned or other inedible poultry products are similar to the meat regulations. They are found in 9 CFR 381.95. Here's a brief summary of this regulation. FSIS inspectors must verify that the establishment disposes of condemned and inedible products using one of the appropriate methods outlined in the regulation.

Condemned and inedible poultry products may be disposed of by one of the following methods.

- Steam (381.95(a))
- Burying (381.95(e))
- Incineration (burning) (381.95(b))
- Chemical denaturing (381.95(c))
- Dye denaturing (381.95(c)(3))

Only burying and burning may be used for products condemned for biological residues.

LINE SPEEDS

Maximum line speeds established by FSIS are permitted on the slaughter or eviscerating line when optimum conditions exist (381.65(a), 381.67, 381.68, 381.76 and 310.1(b) (1)). When there are less than optimum conditions, line speed adjustment is required to ensure that IPP can perform a post-mortem inspection of poultry and livestock carcasses. The IIC is responsible for directing establishment management to reduce the line speed to permit adequate inspection. When the IIC is satisfied that the situation that necessitated the line speed reduction has been corrected, he or she will permit increase in the line speed.

FSIS may require the establishment to adjust line speed to a slower rate than the maximum when process control of line speeds is not maintained because of inconsistencies in size, weight, class of animal or bird, health, pathology, contamination, sanitary dressing or presentation.

Poultry

PHVs or IICs assigned to poultry slaughter establishments are to perform or assign presentation checks using appropriate presentation forms or otherwise assess presentation line speed process control, and evaluate the health status of the flock, as often as necessary. The factors to assess include the following:

- poultry class and the size of the birds in the class
- presentation errors, such as viscera on the wrong side or not presented in a consistent manner
- high level of disease incidence in birds
- establishment personnel's inability to accomplish eviscerating procedures sanitarily with a minimum of contamination
- establishment facilities

FSIS does *not* require line speed adjustments for excessive feathers on carcasses at post mortem inspection.

PHVs or IICs are to assess evisceration line speed control when on–line IPP report to them potential problems with presentation, sanitary dressing, contamination, and pathology or disease status of the birds. If conditions do not allow IPP to perform the proper inspection procedures at a given line speed, PHVs or IICs are to:

- reduce line speeds according to instructions provided on presentation forms (FSIS Form 6510 series) or to a speed at which IPP can perform the proper inspection procedures;
- document the reduction of line speed on a non-compliance record (NR) only when the maximum line speed is exceeded or the allowable number of presentation errors that call for an immediate reduction in line speed is reached. The NR should describe findings that support the reduction in line speed and cite

appropriate regulations (9 CFR 381.76, 381.67, 381.68, and 381.65) under the Other Verification Task in PHIS.

Livestock

PHVs or IICs assigned to livestock slaughter establishments are to perform or assign verifications to determine when the inspection procedures cannot be adequately performed at the current line speed. This could be because of particular deficiencies in carcass preparation and presentation by the establishment at that higher speed or because the health condition of the particular animals indicates a need for a more extensive inspection (9 CFR 310.1(b)(1)). PHVs or IICs should also perform or assign verification activities to determine whether the establishment's slaughter and sanitary dressing procedures are controlling contamination that may impact IPP's ability to perform proper post-mortem inspection procedures. This should be done in conjunction with specific verifications of slaughter line speed process control.

PHVs or IICs are to assess slaughter line speed control in conjunction with sanitary dressing verifications, as appropriate, when on–line IPP report potential problems with presentation, sanitary dressing, contamination or pathology and health status of the animals.

If conditions do not allow IPP to perform the proper inspection procedures at a given line speed, PHVs or IICs are to:

- reduce line speed to a speed at which IPP can perform the proper post-mortem inspection procedures;
- use the Livestock Sanitary Dressing task in PHIS to document noncompliance in accordance with FSIS Directive 6410.1 when the IIC determines there is evidence that the insanitary condition created has resulted in the inability of the on-line IPP to adequately perform the proper post-mortem inspection procedures;
- use the Other Verification Task in PHIS to document noncompliance only when the maximum line speed has been exceeded or when particular deficiencies in carcass preparation and presentation has resulted in the PHV or IIC slowing the line speed. The NR should describe findings that support the reduction in line speed, citing 9 CFR 310.1(b)(1).

PHVs or IICs are responsible for ensuring that each on-line inspector is aware of his or her authority. The PHV or IIC also has the responsibility to regularly correlate appropriate Agency standards and monitor performance for each inspector to assure uniformity of inspection procedures and actions.

MARKS OF INSPECTION

Once the carcass and parts have been passed for inspection, the carcass may be washed, branded, and sent to the cooler. Parts may also be washed. Skimmings from such washing cannot be used for edible purposes.

For livestock carcasses, the marks of inspection are applied just prior to the carcass entering the cooler. Each carcass must contain at least one mark of inspection on each

half before entering the cooler if the carcass is completely split in half. If the sides of the carcass are held together by natural (skin) attachments, one mark of inspection is sufficient. The marks of inspection for meat products are shown in 9 CFR 312. The marks of inspection for poultry products are shown in 9 CFR 381.98. FSIS Directive 6810.2 covers marking meat carcasses and products.

STORAGE AND SHIPPING

Inspection procedures related to the regulatory requirements regarding sanitation and documentation must be performed in relation to product storage and shipping.

Condensation in coolers is a common problem. It is caused by hot air contacting a cold surface and causing moisture to form. It is the establishment's responsibility to prevent product contamination from condensation. If contamination from condensation does occur, the inspector should retain contaminated product and reject the area until the condition is corrected. Any condensation on product is considered to be contamination.

Wooden pallets may be used for temporary in-plant storage of packages or properly protected product provided they are structurally acceptable, clean, and do not contribute to unsanitary conditions or product contamination.

The inspector assigned to coolers, shipping, and receiving may be responsible for officially sealing product being shipped from one official establishment to another. The product may consist of unmarked or restricted inspected and passed product (i.e. Passed for cooking, refrigeration, or other restriction) being shipped in a truck or railcar. The truck or railcar is sealed by a program employee with an official seal. FSIS Form 7350-1, *Request and Notice of Shipment of Sealed Meat/Poultry* is required to identify the shipment to the inspector at the receiving establishment.

Unmarked inspected and passed product intended for further processing may be shipped under official seal from one official establishment to another (316.8). For unmarked product to be shipped under seal, *at least* 25% of the product in the vehicle must be unmarked. This is to prevent the establishment from purposely placing a small amount of unmarked product into each vehicle and having them sealed with an official government seal and warning tag for the purpose of discouraging theft. If the shipment does not meet this requirement for sealing, then all products must be properly marked or labeled. The 25% requirement *does not apply when restricted product is being shipped.*

A vehicle carrying restricted product may be sealed or an alternate method may be used. This method is to pack the product into individual containers, sealing the containers by firmly applying a pressure-sensitive tape around each container in two directions, and then stamping the intersection of the tape with the 2 1/2 inch rubber brand. A U.S Retained tag must be affixed to each container and an FSIS Form 7350-1 used for each shipment.

In many establishments, it is common for product to be returned from unofficial establishments, such as retail stores. In order that the inspection program can control returned product, it must be delivered to this area as soon as practical. The establishment should not sort, remove, or otherwise handle the returned product until it

has been reinspected (318.2). After sorting by the establishment, inspect the product the establishment has elected to save. Any product found to be wholesome and bearing the official mark of federal inspection is released for use to the establishment. Any product found to be unwholesome or unidentifiable is condemned. The product must be accompanied by inspection personnel to be either tanked or denatured.

When unclean or unsound product is received from another establishment the inspector will complete an FSIS Form 8140-1, *Notice of Receipt of Adulterated or Misbranded Product.* This form is executed only when the conditions reflect negligent procedures on the part of the originating establishment, such as kill floor dressing, contamination, rail dust, etc. The form should not be used for conditions that cannot be controlled by the originating establishment. An example of an uncontrollable condition would be off-condition product resulting from failure of the refrigeration unit during transit. The form is intended for internal use of the inspection program and is not to be issued to the establishment. For the FSIS Form 8140-1 to be effective, information entered on it must be specific - the type of contamination, where it was located on the carcasses or parts, and the number or amount of product affected.

Establishments are permitted to ship properly marked or labeled product without an inspector on duty if they have a good history of shipping clean acceptable product in acceptable vehicles. If an establishment continuously receives FSIS Form 8140-1, Notice of Receipt of Adulterated or Misbranded Product, the privilege of shipping without an inspector on duty may be revoked by the Frontline Supervisor
.

POST-MORTEM INSPECTION REPORTS

Inspection personnel must also record information about the number of animals or birds slaughtered, the number and types of products condemned, and other details. The types of reports required are described in FSIS Directive 6100.2, “Post-Mortem Livestock Inspection” and FSIS Directive 6100.3, “Ante-Mortem and Post-Mortem Poultry Inspection”. The data found on the slaughter reports and the poultry post-mortem reports reflects an accurate record of the prevalence of diseases encountered by the food inspectors performing post-mortem inspection.

Example: Poultry Post-mortem Reports

Inspection personnel are required to keep track of the number of poultry carcasses condemned on post-mortem inspection for each condemnation category. This information is collected on the lot tally sheet, FSIS Form 6000-16, at the inspection station. The food inspectors are responsible for the maintenance of the Lot Tally Sheet. During the shift, the “inspector’s helper” records condemnations on the Lot Tally Sheet.

Completing the Documentation on FSIS Form 6000-16 (Lot Tally Sheet) for Poultry Post-Mortem inspection

The PHV or designee (off-line IPP) is to complete the appropriate sections of the Lot Tally Sheet including the:

a. inspection date
b. shift of inspection
c. establishment number
d. specific production (lot number)

e. class of poultry

f. number of condemnations for each category

The Food Inspector gives the Lot Tally Sheet to the “inspector’s helper” at the beginning of each shift. The ”inspector’s helper” records the condemnations throughout the shift. The Food inspector ensures the CSI or designee receives the Lot Tally Sheet at the end of the shift.

At the end of the shift, the lot tally sheets from all on-line inspectors are collected by the CSI or their designee. The CSI will total the condemnations for each condemnation category from the Lot Tally Sheets of the on-line inspectors. They will also record on the Lot Tally Sheet the number of establishment rejects. Establishment rejects are carcasses rejected by the establishment before inspection or re-inspection. These totals are acquired from establishment personnel during the shift.

Enter the information from each Lot Tally Sheet into the Animal Disposition Reporting (ADR) section of PHIS.

Establishment management is responsible for collecting and supplying information to inspection personnel on the total number of live birds and their live weight per lot, and the total pounds condemned at ante mortem inspection. This will include the dead on arrival carcasses (DOAs). Establishment management must also supply inspection with the total weight in pounds of carcasses and of parts condemned on postmortem, and with the total weight in pounds of chilled and frozen product from that lot. Establishment management supplies inspection with these data on FSIS Form 6510-7, the Poultry Lot Information sheet.

All of the above information is to be recorded by the inspector into the ADR section of PHIS. The ADR data is collected and reported on a lot basis for each shift. This means that there may be multiple sets of numbers reported for each shift.

A condemnation certificate must be completed for each lot of poultry slaughtered. The condemnation certificate, FSIS Form 9061-2, is completed and signed by the inspector in charge. The condemnation certificate contains both ante mortem and post mortem condemnation information. The condemnation certificate is generated by PHIS, using the information entered in the ADR section.

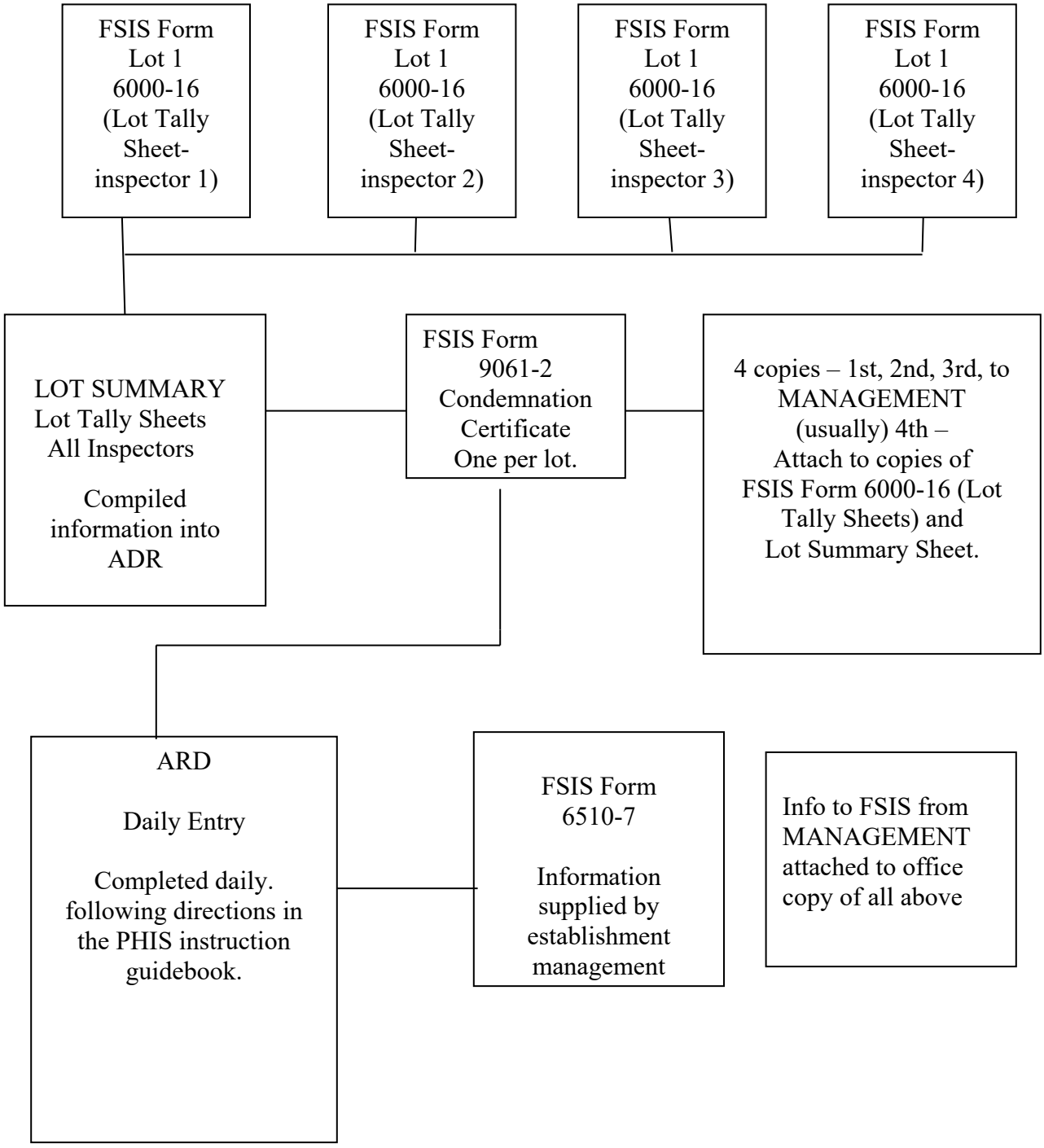
Once all of the required forms have been completed and information gathered, they must be properly filed, entered, and/or distributed, as follows:

1. FSIS Form 6000-16, the lot tally sheets, are kept in the government office attached to the summary for each lot;
2. FSIS Form 6510-7, the Poultry Lot Information sheet from establishment management, is filed in the government office with the other records for each lot;
3. The ADR data is collected and reported on a per-lot, per-shift basis.
4. FSIS Form 9061-2, the condemnation certificate, is distributed as follows: after establishment management signs the form, the first 3 copies are given to establishment management, and the fourth copy is filed in the government office with the other records from each lot.

The following page contains a flow chart of the distribution of all FSIS forms related to postmortem reports.

FLOW CHART FOR POST-MORTEM REPORTS

Example for a Establishment with 4 line Inspectors



APPENDIX

Post-Mortem Inspection Procedures

CATTLE

Head inspection

There are four steps in head inspection.

1. Step one is to observe the outer surface of the head and eyes.

There are some specific conditions that may be identified during head inspection. For example, when inspecting cattle heads, during step one, the observation of the head's surface and eyes, the diseases and conditions that may be detected include contamination (e.g., hide, hair, dirt, rust, and grease), epithelioma, actinomycosis, actinobacillosis, and abscesses.

2. Step two is to incise and observe the four pairs of lymph nodes – mandibular, parotid, lateral retropharyngeal (atlantal), and medial retropharyngeal (suprapharyngeal).

The type of diseases and conditions that may be detected when performing step two (incising and observing lymph nodes of the head in cattle) include tuberculosis, actinobacillosis, epithelioma, and abscesses.

3. Step three is to incise and observe the masticatory or cheek muscles.

The diseases and conditions that may be detected during the performance of step three, incising and observing the masticatory muscles during cattle head inspection include cysticercosis, eosinophilic myositis, bruises, steatosis, and xanthosis.

4. Step four is to observe and palpate the tongue.

The diseases and conditions that may be detected when performing step four (observing and palpating the tongue while performing cattle head inspection) include actinobacillosis, and foreign bodies such as thorns.

You will learn more about what to do when these diseases or conditions are observed when we cover the Multi Species Dispositions module.

Carcass Inspection

Almost all establishments handle the carcass the same way until the time the head is removed. Once the head is removed however, any one of several methods may be used to complete the carcass dressing. Almost all the different methods being used today are variations of two basic operations. One of those basic methods is called a "bed" dress operation. The other is called an "on-the-rail" method was dressing operation. The bed dress method is by far the oldest method and probably date back to the time when animals were "field dressed." This method is still widely used; however, it

is most often used in the low-volume establishments. After the head has been removed, the carcass is lowered to the skinning bed. The skinning bed may be cradle or it may be the floor. The “on-the-rail" method was designed with volume in mind. The animal is moved around the slaughter floor by means of a rail and instead of one employee dressing the entire animal several specialists will perform their jobs as the carcass moves past them.

In either dressing method there are several sanitary dressing requirements you need to be alert to. First, *all* grubs, contamination, bruises, etc., *must* be trimmed from the back of the carcass in the path the saw is to proceed, before splitting.

Secondly, even though it is not required that the saw be sanitized after each use, on normal carcasses, it *must* be sanitized when used on a retained carcass or when a hidden abscess or other pathology is contacted.

The two halves are moved to the carcass (rail) inspection station. The establishment is responsible for assigning an employee prior to the inspection station to trim and remove all bruises, blood clots, grubs, and the like. The establishment employee must *not* remove any abnormality that could affect the disposition of the carcass.

Frequently on the bed dress operation, the carcass will be trimmed and rail inspection accomplished by the viscera inspector while the split carcass is in the same area where it was eviscerated.

After the rail inspection is completed the carcass will be moved, or proceed on the chain, to the final wash area.

Any carcasses located on the "final" rail must be physically separated from other carcasses. This will prevent cross-contamination from one carcass to another. In no case will a retained carcass be washed or trimmed unless authorized by a program employee.

The following steps are those to follow when inspecting the carcasses.

Hindquarter inspection

1. Observe back of skinned carcass while eviscerated.
2. Palpate scrotal (superficial inguinal), or mammary (supramammary), and medial iliac (internal iliac) lymph nodes.
3. Observe body cavities.

Forequarter inspection

1. Observe cut surfaces of muscles and bones, diaphragm's pillars and peritoneum.
2. Observe and palpate kidneys and diaphragm.
3. Observe pleura, neck and carcass exterior.

Carcass inspection

1. Palpate superficial inguinal, or supramammary, and internal iliac lymph nodes. Observe lumbar region.

2. Observe and palpate kidneys.
3. Observe diaphragm's pillars and peritoneum.
4. Observe and palpate diaphragm.
5. Observe pleura, cut surfaces of muscles and bones, neck, and carcass exterior.

You are usually doing two dexterity actions during each step. For example, you may be required to *observe* and *palpate*, or *incise* and *observe*.

If you observe a disease or condition that requires you to retain a carcass, tag each half-carcass, request that the viscera and head be retrieved, and apply one tag to each.

Products, parts, etc., that are removed and condemned for various reasons are usually placed in a container near the rail inspector and the viscera inspector. These containers must be properly identified for their intended purpose. The inspector who is responsible for the area where the containers are located must also be responsible for seeing that the containers are either locked, sealed with an official seal, or under visual security at all times. You would not leave the area before the container was locked or sealed. We will cover this in more detail later during this module.

In most operations, a final inspection rail or final disposition room is located immediately following the rail inspection station. The rail inspector must be alert to require that *all* carcasses that need a final inspection by the veterinarian or further trimming to insure they are wholesome, are removed to this area.

Viscera Inspection

Viscera separation is the dividing of the internal organs of the body such as the heart, lungs, liver, kidneys, intestines, etc., into various offal products. Offal parts are animal parts other than the carcass (body).

The following steps are performed in viscera inspection.

1. Observe cranial and caudal mesenteric (mesenteric) lymph nodes, and abdominal viscera.
2. Observe and palpate rumino-reticular junction.
3. Observe esophagus and spleen.
4. Incise and observe lungs lymph nodes - mediastinal [caudal (posterior), middle, cranial (anterior)], and tracheobronchial (bronchial) right and left.
5. Observe and palpate costal (curved) surfaces of lungs.
6. Incise heart, from base to apex or vice versa, through the interventricular septum, and observe cut and inner surfaces.
7. Turn lungs over; observe ventral (flat) surfaces and heart's outer surface.
8. Incise and observe hepatic (portal) lymph nodes.
9. Open the bile duct (both directions) and observe its contents.
10. Observe and palpate liver's ventral surface.
11. Turn liver over, palpate renal impression, observe and palpate parietal (dorsal) surface.

Here are some further details about viscera inspection.

Inspection of the Abdominal Viscera

Abscesses are frequently detected during the palpation and observation of the rumino-reticular junction. These abscesses are usually localized and required only that the viscera be condemned. You should be alert though, to the overall condition of the carcass, and thoracic viscera. If abscesses are found in other locations, in addition to the abdominal viscera, it could be an indication of a generalized condition, in which case you would retain the carcass and all parts for the veterinarian to make a final disposition.

The mesenteric lymph nodes may show evidence of tuberculosis, neoplasms, and in some cases pigmentary color changes.

You must retain the carcass and all parts when you detect tuberculosis and tumors.

Most pigmentary color changes in the lymph nodes may be due to the animal's age or the environment in which the animal has been maintained and is usually of little concern. As with all abnormal conditions, though, if you were unsure of the cause or involvement of a condition, you would retain the carcass and parts for the final disposition by the veterinarian.

The small intestines may appear dark red to purple; this would indicate a condition called enteritis. The determination whether the condition is acute or chronic must be made.

There are several other conditions detectable at the time you observe the abdominal viscera. These may vary from a slight redness or odor in the uterus or pyometra (metritis), to a retained placenta or fetus. In these instances, you should evaluate the degree of involvement, the remaining viscera condition, the condition.

Evidence of adhesions may be seen. Again, if the condition appears localized, or chronic, and no further carcass or viscera involvement is observed, the abdominal viscera would be condemned and the carcass retained for trimming.

Inspection of the Spleen

The inspection of the spleen is done by observation. If tuberculosis is suspected, the carcass and all parts will be retained for veterinary disposition. You will see physical differences between normal and abnormal. There may be a definite swelling or size difference, or a color difference. When an abnormal spleen is detected, retain it as well as the carcass and all parts. The spleen may be helpful in making a final disposition on any carcass. Ensure that the spleen is included with the viscera whenever a carcass is retained for a disease condition.

Inspection of the Esophagus

Observe the esophagus for *Cysticercus* (measles); eosinophilic myositis (EM); and evidence of grub infestation. *Cysticercus* and EM conditions require retention. Grub infestation is usually a localized condition requiring affected organs and areas be trimmed or condemned, but the carcass will usually be passed without retention

Inspection of the Pluck (Lungs and Heart)

Pneumonia and pleuritis are the most common abnormalities observed. Acute pneumonia is characterized by enlarged, edematous lymph nodes and/or dark red to purple sections or spots in the lung tissue. Retain this carcass and all parts for disposition.

A chronic pneumonia may be characterized by a localized abscess within the lungs, or many times evidence that the lung has become adhered to the pleura (lining of the thoracic cavity), frequently called pleuritis. Observe the rest of the viscera and carcass to look for evidence that the condition is generalized. For example, you may detect other sections of the carcass with swollen lymph nodes, or other adhesions. The carcass may appear degenerated. There may be water tissue, fat sloughing, etc. Any of these would indicate a generalized condition. You will retain the carcass and all parts upon detecting a generalized condition. When the condition is strictly localized, the lungs would be condemned, as well as any contaminated organs, and the carcass retained for removal of the adhesions.

Tuberculosis may also be detected during incision of the lung's lymph nodes. When TB lesions are detected, the carcass and all parts must be retained.

Another condition you may detect while incising the mediastinal lymph nodes is the thoracic granuloma. A granuloma may appear as an abscess or pus pocket in the lymph node. Retain the viscera, especially the pluck, for disposition. You may collect and submit samples of the granuloma lesion. The granuloma could be TB related. We will cover this in more detail during the module on Multi Species Dispositions.

Neoplasms (tumors) may be detected during palpation of the lungs. These tumors would appear as nodules or lumps in or on the lung tissue. The carcass and all parts would be retained.

Inspection of the Heart

The inspection of the heart involves opening it by an incision form the base to the apex, or vice-versa. The usual procedure is to position the heart in a manner that will allow you to safely cut away from your body, and incise the left ventricle about an inch and one-half posterior to the lefts of large vessels leading into the chamber. Then grasp the opened edge of the ventricle and incise the septum. By rotating the knife 180 degrees with the cutting edge pointing up, complete opening the ventricles and great vessels with two incisions, causing the heart to lay flat or open.

In some establishments, the heart may be inspected without being opened. If this is the case, a company employee must invert the heart for you to complete your inspection, and you would normally make a slight incision in the septum walls in addition to observing the inner heart surfaces. This procedure is difficult except on older animals, where the heart muscle is thinner and more pliable. The company employee will also re-invert the heart for you to observe the heart's outer surface.

Some of the conditions you may detect while inspecting the heart include:

Cystircercus (tapeworm cysts, measles, etc.)
Eosinophilic myositis (EM)

Neoplasms (tumors)

Pericarditis is an inflammation of the pericardium or heart sac. When an inflammation of the inner lining of the heart occurs, the condition is referred to as endocarditis.

Inspection of the Liver

Liver Abscess

An abscess is a circumscribed area of pus with related swelling and/or inflammation caused by a variety of factors. Abscesses may be associated with specific diseases, but are usually seen as localized conditions. Many feedlot cattle (fat) have localized abscesses and the cause seems to be related to high-energy cereal diets, with unsanitary feedlot conditions also a factor. An abscess may appear on the surface and be quite obvious, or it may be located under the surface, and only detected when you palpate properly. (You must remember to palpate deeply to detect hidden or invisible conditions.) You may make as many incisions as you feel necessary to search for abnormal conditions, but remember you should not mutilate product unnecessarily. In *all* cases, a liver containing an abscess is condemned as not fit for human consumption. Benign abscesses (non-malignant, and judged *not* to be affecting surrounding tissue) may be salvaged for animal food *after* removal of the abscess itself.

"Sawdust" and Telangiectasis (Telang)

The condition in which a liver has pinkish-white to yellow-gray necrotic (dead) spots that make the liver appear as if sawdust had been sprinkled or scattered through it is called "Sawdust." The area around the spots appears normal and the liver's surface over the spots is usually smooth. The condition in which a liver has purple-red to bluish-black spots present both on the surface as well as throughout the organ is called telangiectasis and is referred to as "Telang." Usually the surface of the liver is slightly depressed when affected with Telang.

To determine the disposition of sawdust and Telang conditions, *three* degrees of involvement are used.

1. Slight: Where the lesions are small in size and slight in number. A liver meeting the slight criteria is passed for food without restriction.
2. More severe than slight but involves *less* than one-half of the organ: The portion of the liver that is *not* affected or only slightly involved may be passed for food without restriction, while the remainder of the liver is condemned.
3. More severe than slight and involves *more* than one-half of the organ: The entire organ is condemned. (It may be salvaged for animal food.)

Liver Flukes (Distoma)

The appearance of a fluke infested liver depends a great deal on the amount of fluke infestation. A slight infestation will probably not affect the liver tissue as such. A heavy infestation may cause a cirrhotic effect on the organ, with the surface becoming scarred. Many times there are bumpy, raise and/or depressed areas, and sometimes a discoloration showing dark blue to black sections on and within the tissue. The liver may take on a "hobnail appearance."

The primary purpose in opening the bile duct during liver inspection is to detect flukes. When there is a fluke infestation the bile duct may be thickened and sometimes swollen; frequently you will observe live flukes. The three liver flukes most often seen in domestic cattle today are: *Fascioloides magna; Fasciola hepatica; Dicrocoelium dentricum* (Lancet).

In all cases of liver fluke infestation the liver is condemned and not eligible for human consumption. The liver *may* be salvaged and used for animal food.

Carotenosis

A liver with carotenosis is characterized by a highly colored yellow-orange color or pigmentation. This condition is quite common in cattle livers and may cause the liver to become enlarged, soft, and friable (easily crumbled). Here's a practical test to assure the correct recognition of carotenosis. The test is made be placing a white paper towel or napkin on the cut surface of a liver suspected of being affected with carotene discoloration. An orange-bronze stain would be indicative of carotenosis. The liver is condemned and not eligible for use a human food but *may* be salvaged for animal food uses. The pale-colored liver found in near-term cows may resemble carotenosis. For this reason you must be sure of your diagnosis. The pale liver may vary from tan to yellow to gray in color and may be enlarged. Usually the cut surface feels greasy. The cause of this pale liver is thought to be the result of a change in fat metabolism of the near-term cow. Livers from cattle that are normal except for the pale color are passed without restriction.

Hydatid Tapeworm Cyst

Hydatid cysts may occasionally affect livestock. Most domestic food animals are the intermediate host for this tapeworm cyst, which usually is a result of the tapeworm (*Enchinococcus granulosus*) of dogs. While the animal eats or grazes, it consumes the eggs, probably deposited by the dog, and the eggs in turn change to larvae in the food animal's system. The larvae then end up in various organs via the blood stream.

The cyst will vary in size but may be as large as two to four inches in diameter. The fluid inside the cyst is usually clear and colorless. You must be careful not to confuse the hydatid cyst with an accessory gall bladder.

The organ or part affected with a hydatid cyst is condemned and is *not* suitable for use in animal food.

Control of Condemned Livers

Those livers that *are* condemned, but which the company has indicated it wishes to salvage for animal food, must be handled properly before they may be shipped from the establishment as animal food livers. Here is a summary of the steps to take.

1. The livers must be marked "U.S. Condemned."
2. The condemned livers may be held in containers on the slaughter floor, or may be worked as inedible product during the slaughter procedure.

a. When the condemned livers are placed in a container, the container must be plainly marked "inedible." Ensure that the product in these containers is maintained under security at *all* times. This means under you direct supervision, or locked or sealed in a container with an official device until such a time that the product *is* properly denatured.
b. When the establishment requests an opportunity to slash and denature the condemned livers during the slaughter operation, it *may* be done, provided it doesn't create problems of control, security, or contamination.

Liver Disposition Chart

Disease or Condition	Degree	Disposition
Telangiectasis Sawdust Spotted	Slight	Pass for human food
	The affected portion trimmed when less than 1/2 of liver is more than slight	Condemn/Use for animal food
	Balance of this liver is slight or less	Pass for human food
	More than slight involving 1/2 or more of liver	Condemn/Use for animal food
Contamination	Excessive	Condemn/Tank
Cirrhosis	Any amount	Condemn/Use for animal food
Nonmalignant change	Any amount	Condemn/Use for animal food
Abscesses-benign (trim)	Localized - Affected area	Condemn/Tank
	Localized - Non-affected area	Condemn/Use for animal food
Flukes	Any evidence of infestation	Condemn/Use for animal food
Hydatid Cyst	Any amount	Condemn/Tank
Abscesses (Not benign)	More than localized	Condemn/Tank
Carotenosis (yellow)	Any amount	Condemn/Use for animal food
Other Parasites	Numerous lesions and cannot be removed	Condemn/Use for animal food
	Localized: Affected area trimmed	Condemn/Use for animal food
	Localized: Non-affected area	Pass for human food

References: Regulation 311.25; 311.31, and 314.10

Presentation

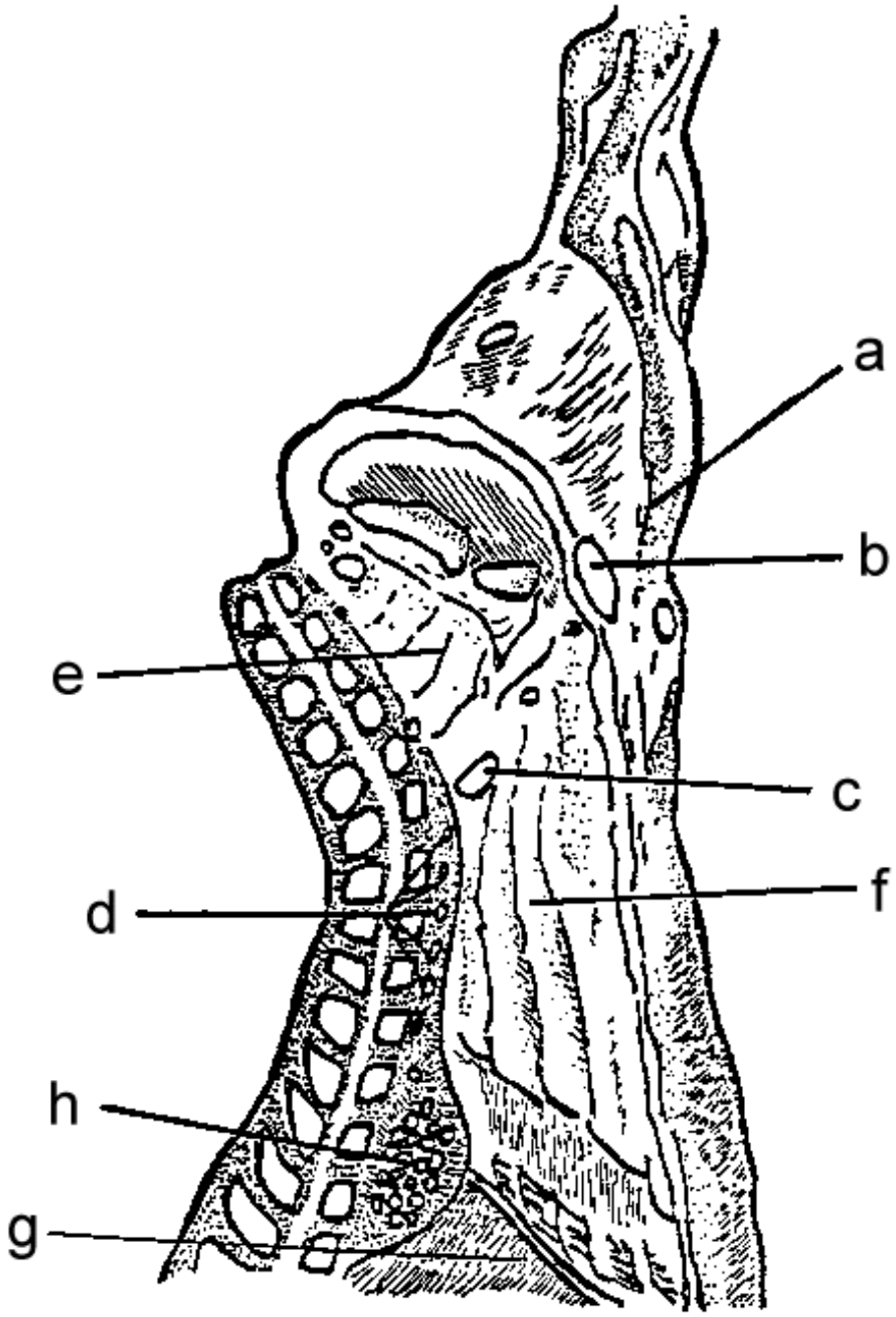
During the evisceration procedure several improper presentations may occur. The following are examples:

- The liver may be placed with the parietal surface up.
- The hepatic (portal) lymph nodes may be missing from the liver.
- The bladder may be leaking urine onto exposed surfaces of the carcass or viscera.
- The paunch or intestines may be cut or broken, causing contamination.
- The pluck may be placed upside down, i.e., the ventral surfaces of the lungs pointing up.
- The liver, pluck, and viscera, or any one of these organs, may be pushed to or deposited on the opposite side of the table from your station, or literally missing.

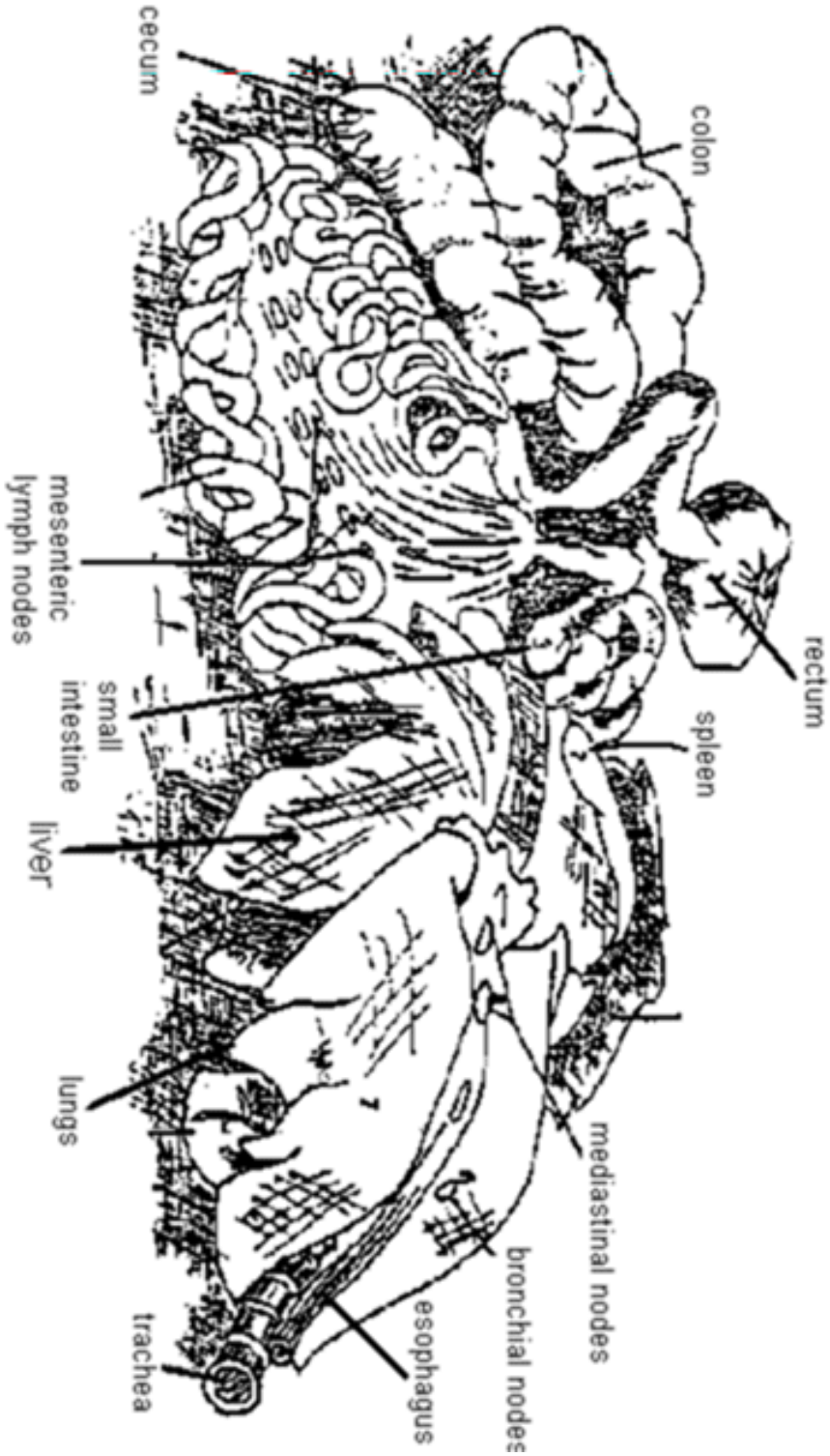
There are many other examples of improper presentation. Generally, if an improper presentation occurs infrequently, delay inspection long enough to complete inspection duties. Also require that any contamination be removed. *A very important consideration*

is that your attention to the actual inspection procedures must not be distracted. You may miss something you need to see.

If any improper presentations occur frequently, delay inspection, and meet with establishment management in an effort to get the problem(s) under control. *Your attention must not be distracted during the inspection procedure.*



LIVESTOCK ANATOMY SCHEMATICS



CALF INSPECTION

Calves of all sizes and ages are slaughtered. Some establishments slaughter "bob veal" calves. These calves are defined as, “under 150 pounds and less than three weeks of age”. Although it is beyond the scope of this module to cover bob veal slaughter in detail, there are some aspects of these operations of which you should be aware. Historically, these very young calves have been a serious source of residue violations, particularly sulfa residues. Because of this, much of the work in establishments that slaughter bob veal calves involves the use of rapid in-plant tests to detect sulfas and antibiotics. The FAST test is used to detect residue violations. Should you be assigned to a bob veal operation in the future, become familiar with the statistical sampling plans and tests used.

Beyond three weeks of age, definite guidelines or definitions for what size constitutes a calf are not in FSIS publications. Some regions have established policies for size limitations on calves. This is important because inspection procedures for calves are not nearly as complete as those for mature cattle. It is important to note that large calves require an expanded inspection procedure that is identical to that for cattle inspection. This is because some abnormal conditions, such as measles (Cysticercosis), require a certain amount of time to develop. If in doubt about whether to use calf or cattle inspection procedures, it is essential to check with your supervisor to assure you perform the appropriate procedures.

Calves are dressed by one of two methods. Calves may be hot skinned. This method is essentially the same used for other livestock. The hide is removed on the kill floor at the time of slaughter. Alternatively, calves may be cold skinned. This is also referred to as dressed "hide-on." In this method the hides are not removed on the kill floor but rather in the cooler after the carcasses have chilled.

It is said that cold-skinned calves maintain their "bloom" (the bright red appearance of freshly dressed, properly chilled carcasses and meat) and shrink less than hot-skinned calves. This is because the hide prevents loss of moisture from the carcass during the chilling process, resulting in less weight loss.

<u>Hot skinning</u>

The same basic sanitary dressing requirements that apply to cattle are applicable to hot-skinned calves. They include:

- Daily cleaning of the knocking box.
- Keeping the animals as dry as possible.
- Not bleeding in the dry landing area if possible.
- Clean head skinning and removal (head with carcass identification).
- Sanitary hide and feet removal.
- Bung and bladder tying as necessary.
- Sanitizing brisket opening device between each use

Establishment management is responsible for handling all carcasses and parts in a sanitary manner regardless of the dressing method used.

Cold skinning or Hide on

The carcass (hide) must be completely clean of dandruff, dirt, and fecal material before heading or opening of the carcass. Cleaning is sometimes facilitated with "curry combs" or other scraping instruments, and always with potable water. There needs to be sufficient water pressure, volume, and a competent washer to accomplish complete cleaning. There is one exception to the rule that cleaning of the hide must precede heading or opening of the carcass. Should you ever be assigned to an establishment where Kosher slaughter is performed, you will note that the head may be removed before the hide is washed.

Monitoring the spacing of carcasses is a very critical point. After removal from the carcass, the head is thoroughly washed and the cavities flushed in the same manner as cattle heads (this is true of hot-skinned calves also). The head is then placed on a rack or hook for inspection. As in other species, when the head is removed from the carcass a method of identification acceptable to the IIC is necessary to assure that the identity of the head and its corresponding carcass is maintained until inspection is complete.

Some establishments may wish to save calf tongues but do not want the rest of the head and therefore do not want to expend the effort to skin the head. This is acceptable provided:

- the head is washed,
- medial retropharyngeal (suprapharyngeal) lymph nodes are exposed for inspection, and,
- tongues are washed individually

The hide is then opened and skinned back on the hock just far enough to allow insertion of the gambrel. The lower leg with the hide attached can then be removed. The front side of the hock should not be skinned until the hide is completely removed. *The hock is not to be exposed until final skinning.*

Next, the front feet are removed. Note that all procedures to this point have been performed prior to any opening being made in the carcass.

Brisket splitting, bung dropping, belly opening, and evisceration must be consistently done in a sanitary manner. Splitting the brisket may be done with a knife, saw, or other acceptable instrument. Whatever device is used, it must be sanitized following each use. The person opening the belly must take care to prevent unnecessary contamination of the carcass.

Bung tying in large calves is done as in cattle, i.e., the bung and bladder must be tied before evisceration unless the urinary bladder is removed and the bung does not cause contamination. The procedure in small calves is similar to that in sheep. The bung and bladder are grasped and the large intestine preceding the bung is stripped. The bung is severed and the bung and bladder are removed.

Now the carcass is ready to be eviscerated. Following evisceration, the viscera (abdominal viscera and pluck) are placed into a tray or truck for inspection.

Hot skinned calves

A. Head Inspection

1. Observe head's surfaces.
2. Incise and observe medial retropharyngeal (suprapharyngeal) lymph nodes - left and right.

B. Viscera Inspection

1. Observe and palpate lungs' lymph nodes [tracheobronchial (bronchial) and mediastinal], costal (curved) surfaces of the lungs, and the heart.
2. Turn lungs over and observe ventral (flat) surfaces.
3. Observe spleen.
4. Observe and palpate dorsal surface of liver.
5. Turn liver over, observe ventral surface, and palpate hepatic (portal) lymph nodes.
6. Observe stomach and intestine.

C. Carcass Inspection

1. Observe outer and cut surfaces.
2. Lift forelegs and observe neck and shoulders.
3. Observe body cavities.
4. Observe and palpate medial (internal) iliac lymph nodes and kidneys.

Cold skinned hide-on calves

In addition to the above inspection procedures, inspection procedures of "hide-on" carcasses must include observation of the hid for contamination, parasitic conditions and other abnormalities, and palpation of the back for grubs. The skins of bruised calves and those affected with grubs, lice, warts, ringworm, and other skin conditions, as well as those found unclean, must be removed as part of the dressing operations at the time of slaughter. In all cases, skinning of calves must be done in a sanitary manner and un-skinned carcasses must be adequately spaced.

Large calves

Recall that large calves require the same inspection procedure described for cattle. This expanded procedure is necessary on large calves because their age may have permitted abnormal conditions such as measles (*Cysticercosis*) to develop. Improper presentation of carcasses or viscera (such as dirt, hair, hide, ingesta, grease, pus, etc.) may occur as in other species. When this occurs, action must be taken by the inspector to correct the problem. Actions taken will depend on the nature and frequency of dressing errors. If in doubt about what actions need be taken, review the cattle and swine inspection modules for assistance.

Calf Post-mortem Pathology

When abnormal conditions are encountered on calf inspection, the proper reaction is to retain the carcass and parts for veterinary disposition, or retain just the carcass if only hide removal and/or extra trimming is necessary for the carcass to pass inspection. A two-section retain tag is usually used by placing one section on the carcass and one on the viscera if the carcass, head, and viscera are retained. The corresponding head is retained by use of the head-carcass house identification tag. If only the carcass is retained, both retain tags should be placed on the carcass. The large retain tag (US Retain/Reject tag) may be used to retain carcasses for dirty hides. Should you be assigned to a calf slaughter establishment you must become familiar with whatever means are utilized to identify retained carcasses and parts.

Calves are subject to disease and abnormalities as in other species, while some are unique to calves. A few examples of abnormal conditions that might be encountered include:

- Abscesses
- Pneumonia
- Nephritis
- Ringworm - This condition should be detected on ante mortem inspection. It is significant in hide-on calves and would require removal of the hide at the time of slaughter.
- Warts - See Ringworm.
- Grubs - Another hide condition that requires skinning the carcass. Grubs are the larvae of the heel fly, which infects cattle. The primary reason for palpating the backs of calves at postmortem inspection is to check for the presence of these parasites.
- Arthritis
- Icterus - The carcass and parts have a yellow appearance. In true icterus, normally white tissues (such as the tendons and sclera of the eye) are affected.

After carcasses are cold-skinned in the cooler, they must be examined for injection lesions, foreign bodies, parasites, bruises, or other pathology not detectable with the hide still on.

SHEEP AND GOAT INSPECTION

Viscera Inspection

1. Observe abdominal viscera, esophagus, mesenteric lymph nodes, and omental fat.
2. Observe bile duct and content and express gall bladder.
3. Observe and palpate liver (both sides) and costal surfaces of lungs.
4. Palpate bronchial and mediastinal lymph nodes.
5. Observe ventral surfaces of lungs.
6. Observe and palpate the heart.

When certain disease conditions are found, the viscera and carcass will be retained for the veterinarian's final disposition. The usual procedure for tagging is to use two small retain tags, each having identical serial numbers. One tag is attached to the viscera, and the other tag to the leading side of the carcass on the hind leg.

When an unacceptable or improper presentation occurs, you must evaluate the situation and require the establishment to take action you consider necessary. For example, a sheep pluck covered with paunch content is presented to you for inspection. You have been working the assignment all day and this is the first incident to occur today. You would delay your inspection of that pluck until it was cleaned up adequately for inspection. However, it the same situation was occurring frequently, you would have to stop the line and inform establishment management the problem had to be corrected.

Carcass and Head Inspection

1. Observe outer surfaces of carcass, body cavities (pelvic, abdominal, thoracic), and spleen.
2. Observe and palpate kidneys.
3. Palpate sub iliac, scrotal or mammary, and deep popliteal lymph nodes.
4. Palpate back and sides of carcass.
5. Palpate superficial cervical lymph nodes and shoulders and lift forelegs.
6. Observe neck, shoulders, and head.

Following are some of the more common disease conditions in sheep.

- Caseous lymphadenitis – a bacterial infection results in a disease that produces inflammation and resulting caseous (cheese-like) abscesses in lymph tissue. Retain for veterinary disposition.

- Tapeworm - a parasite found in the gall bladder and bile ducts (and occasionally pancreatic ducts). Livers affected with this parasite are condemned for human food; may be salvaged for pet food as an inedible product, provided they are properly handled.

- Nodular worms (*Oesophagostomum* species) – a parasite that produces pea-sized firm nodules on the surface of the small and large intestine, may be associated deterioration of the carcass (thinness, a poor carcass, or an otherwise run-down condition). Retain for veterinary disposition.

- Thin-necked bladder worm - large (3/4 inch or 2 cm), fluid-filled, clear cysts, usually attached to the surfaces of the liver, intestines, mesentery, and omentum. They are frequently also seen in the pelvic cavity. May take the form of an active (live) larva (clear soft cyst membrane and clear fluid contents) or may be degenerated (dead) and appear as firm nodules with a scar tissue or calcified consistency. Condemn organs affected with this parasite and have the pelvic cavity trimmed of any affected tissues, again after correlating with your supervisor.

- Sheep measles (*Cysticercus ovis*) – a parasite is similar to the measles found in cattle because it is found in muscle tissue such as the heart, diaphragm, esophagus, or carcass. The cysts are small (about 1/4 inch of 0.6 cm) and may appear as active, clear fluid-filled cysts or the degenerated firm nodules as described above for the bladder worm. Retain for veterinary disposition.

- Hydatid cysts – cysts are approximately 2-4 inches (5-10 cm) in diameter and may be multi-compartmented, with a white, thick-walled cyst membrane that contains an amber clear fluid that may contain sand-like granules. Occasionally, this thick white membrane will have a very slight clearing of the cyst wall, making it almost transparent. The cysts are most often seen in the lungs and/or the liver. The affected tissues must be condemned to tankage and never allowed for use in pet foods as is allowed with other parasitized product (9 CFR 314.10(a)).

- "Sarco" (*Sarcosporidiosis* sp.) - flat, white parasitic cysts are imbedded in muscle tissue (esophagus, heart, carcass, etc.), having a "rice grain" appearance and being "cigar-shaped bodies" about 1/4 inch (0.5 cm) long. Retain the carcass for veterinary disposition.

- Neoplasia, tumors - growths that can be bizarre or subtle changes of size and/or color of tissues and organs. Retain the carcass and parts for veterinary disposition.

- Pneumonia - an inflammatory disease in which the normal soft "foamy consistency" feel of the lungs and their normal "light-pinkish" color are changed. The color change may vary from a bright red, to reddish-brown, to brown, to gray, to white. The change in the consistency or feel of the lung may vary from the normal "foamy feeling" to firm (slightly or moderately or markedly). These changes may be accompanied by the occurrence of abscesses in the lung tissue itself or in the lung's lymph nodes. Retain the carcass for veterinary disposition.

- Nephritis - kidneys appear enlarged (swollen) or may be partially shrunken with a gristle-type scar tissue in the kidney tissue. Abscesses may be present. Petechiation, a hemorrhage from a small blood vessel, may be observed. The color change may vary from the kidney's normal color to pink, to blood red, to brick-red, to yellow or amber, to dark brown, to almost black. Various-colored radiating streaks can sometimes be seen on the kidney's surface in certain disease states. Retain for veterinary disposition.

- Abscesses - when this condition is localized, condemn the affected area and pass the reminder of the carcass. However, when it is not localized, retain the carcass and viscera for veterinary disposition. When an abscess has been cut into or

opened, there is a real possibility that other parts of the carcass have been contaminated by this pus. Carcasses so contaminated must be trimmed to your satisfaction before you allow it to pass. If the establishment can accomplish this with a minimum of interference to their operations and you find their solution acceptable, you can allow operations to proceed; however, if not, you must delay your inspection (or stop operations if necessary) until the problem is corrected.

- Arthritis - inflammation of the animal's joints. These are often infected and should not be opened (cut into) on the line. The affected joints will be enlarged and regional lymph nodes generally also are enlarged and may be discolored. Several joints may be involved (polyarthritis), particularly in lambs. Other disease conditions may complicate arthritis, such as septicemia, toxemia, or pyemia. Retain for veterinary disposition.

- Emaciation - fat tissue loses its normal white color and semi-firm consistency and becomes a darker color (almost brown), with a jelly-like to fluid-like consistency. Fat around the heart seems to be the first area of the body affected. Retain for veterinary disposition, but if only the fat around the heart is affected, don't retain the carcass and viscera.

- All localized conditions like bruises, contamination, adhesions, etc., are to be removed by a establishment employee before the carcass enters the cooler. An exception is made in the case of "wild oats," otherwise known as "needle grass or grass awns." These are slender barbed bristles that are a part of the cereal grasses, which become embedded in the subcutaneous tissues of sheep as they graze on pasture. They are black or brown wooden-like slender awns about one-half the size of a wooden toothpick when seen on the carcass. They often can be seen but usually are readily palpable. They are not noticeable on the live animal. They are found generally in the subcutaneous tissues over the abdomen (belly) and the thorax (chest) and occasionally on the back and legs. They are found only in certain parts of the country and therefore most lots are totally unaffected. When they are encountered on the production line the carcasses are trimmed, but when they are trimmed depends on how extensively the carcasses are affected and the proportion of carcasses in the lot affected and the establishments' history of cooperation in correcting the problem. If many of the carcasses (a high proportion) are affected and/or those affected carcasses have numerous grass awns in the tissues, FSIS will allow these carcasses to go into the cooler and be trimmed after cooling if the establishment will segregate or group all affected carcasses in one cluster. Further, if the establishment does not cooperate in this provision, then they must trim all affected carcasses in the presence of the FSIS inspector and before each carcass is passed. If there are just a few grass awns on affected carcasses and only a few (a low proportion) of these affected carcasses in the lot, the establishment should trim affected carcasses before they enter the cooler.

This module has not referred specifically to the slaughter and inspection of goats. Since the requirements and inspection procedures in goats are identical to those of sheep, the information on sheep contained herein can be extrapolated to goats.

RATITE INSPECTION

General Information

Ratites are flightless birds with small wings and flat breastbones. The name “ratite” is derived from the Latin word “ratis”, meaning “raft”, describing the shape of the sternum. The sternum of ratites has no keel, is convex to the outside, concave to the inside, and has a somewhat “raft-like” shape. Ostrich, emu, and rhea are members of this family. Ostrich is native to Africa. Emu is native to Australia. Rhea is native to South America. When fully grown, ostriches, which are the largest birds in the world, stand about seven to eight feet tall and can weigh 300 to 400 pounds. Emu are 6 feet tall and weigh 125 to 140 pounds. Adult rheas are 5 feet tall and weigh 60 to 100 pounds. Ratites are long lived. Ostriches can live to seventy years of age, with hens producing eggs for forty years. All ratites have acute hearing and keen eyesight. Their peripheral vision is almost 360°. Although they are unable to fly, they are excellent swimmers and are extremely agile. They have been around for 80 million years.

Ratite meat is available in innovative restaurants and some meat markets. They are the latest in meat products. The birds are 95% usable as meat, feathers, oil, and leather. It is lean and tastes like beef, but contains much less fat. Ratite meat is even lower in calories than chicken and turkey. Ratites are slaughtered at 10-13 months of age. Even though ratites are poultry, they are classified as “red” meat since the pH of their flesh is similar to beef. The raw meat is very dark cherry red. After cooking, the meat looks like beef and the flavor is similar, but a little sweeter. Ratite meat is sold as steaks, fillet, medallions, roasts and ground meat. The most tender meat comes from the thigh or “fan”. Meat also comes from the drum and forequarter. Emu, ostrich, and rhea meat are considered specialty items.

Post-Mortem Inspection

A careful post-mortem examination and inspection will be performed on the carcasses and parts of all ratites slaughtered at official establishments. The purpose of post-mortem inspection is to make a decision about the wholesomeness of each ratite carcass inspected. One of the following outcomes will result from post-mortem inspection, the wholesome is passed, the unwholesome is condemned, and anything questionable is retained for veterinary review. The PHV is responsible for uniform dispositions made on carcasses presented to food inspectors.

If the carcass is wholesome, except for some localized disease condition, it is allowed to continue unrestricted after removal of the affected areas. The diseased portion that is removed is handled the same as any other condemned material. If the carcass is considered unwholesome, the entire carcass is condemned.

The factors to be considered at post mortem exam include:

1. At the time of slaughter, is there evidence that the disease process is being resolved?
   **If it is being resolved it will show evidence of healing. This will be evidenced by connective tissue walling off lesions, minimal evidence of inflammation, and a return to functional activity of the tissues.*

2. Is there evidence that the disease process is remaining about the same?
   **In chronic conditions, there will be areas of active inflammation, areas of inactivity, or areas of connective tissue representing a granulomatous reaction. Function will still be present in the affected tissues*.

3. Is there evidence that the disease process has developed into an irreversible stage?
   **The lesions of the irreversible stage of an interrupted disease process represent extensive degeneration of parenchymatous organs. Classical signs of septicemia/toxemia (systemic change) are present. The bird would not have recovered from the disease if allowed to live.*

Localized lesions are restricted to a limited region or to one or more spots. The bird's immune system is able to keep the disease or condition confined.

Generalized lesions are systemic, affecting major organ systems. The physiologic functions of the interdependent organ systems are disrupted. The cells of the body are deprived of adequate maintenance to support normal function and they deteriorate. This deterioration may be very rapid when highly virulent microorganisms are the cause, or it can be more gradual if less virulent ones are involved.

Post-mortem Procedure

1. A careful post-mortem examination and inspection will be performed on the carcasses and parts of all ratites slaughtered at official establishments.

2. The heart is incised by establishment employees through the interventricular septum. The heart is observed and palpated by the inspector. The lungs are observed and palpated on all external surfaces. The abdominal and thoracic air sacs are observed.

3. The liver and spleen are observed and palpated.

4. The kidneys are observed with the carcass, then removed to an inspection tray and observed and palpated.

5. All other visceral organs are observed.

6. The neck, trachea, and esophagus are observed.

7. The head, eyes, and sinus openings are observed.

8. Internal and external carcass surfaces are observed.

9. Any carcass or viscera exhibiting abnormal physiological or pathological characteristics shall be tagged "U.S. Retained" and railed out for final inspection by a Public Health Veterinarian.

10. Each inspected carcass and all organs and other parts of carcasses which are not found to be adulterated will be passed for human food. The liver, heart, gizzard, and neck are considered edible byproducts if handled and processed in

a sanitary manner. Ratite kidneys are presumed to concentrate heavy metals and therefore are condemned.

11. Each individual carcass is properly washed immediately after being passed for wholesomeness. Following final washing, carcasses are promptly chilled.

12. Official marks and devices to identify inspected and passed products of ratites are found in 9 CFR 381.96.

US010028915B2

(12) **United States Patent**
Furo et al.

(10) **Patent No.: US 10,028,915 B2**
(45) **Date of Patent: Jul. 24, 2018**

(54) **POLYVINYL ALCOHOL PARTICLES, PHARMACEUTICAL BINDER USING SAME, PHARMACEUTICAL TABLET, SUSTAINED-RELEASE PHARMACEUTICAL TABLET, AND METHOD FOR PRODUCING POLYVINYL ALCOHOL PARTICLES**

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A61K 9/16 (2006.01)
A61K 31/155 (2006.01)
C08J 3/12 (2006.01)

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CPC ***A61K 9/2027*** (2013.01); ***A61K 9/1635*** (2013.01); ***A61K 9/1682*** (2013.01); ***A61K 31/155*** (2013.01); ***C08J 3/12*** (2013.01); *C08J 2329/04* (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

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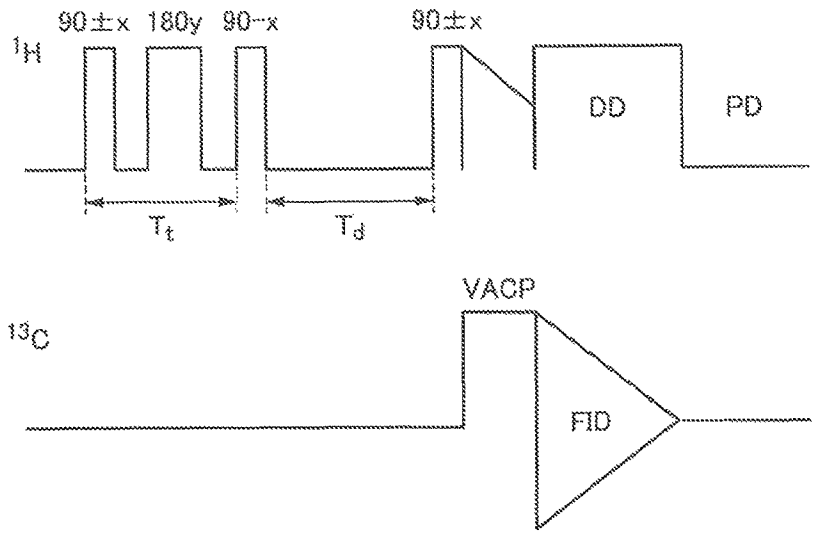
(57) **ABSTRACT**

Provided herein is a polyvinyl alcohol fine particle suitable for a pharmaceutical binder for obtaining a pharmaceutical tablet of properties including good sustained release, high hardness, and excellent friability. The polyvinyl alcohol fine particle of the present invention contains 25 mol % or more of a gauche structure in polyvinyl alcohol molecules within a 0.8-nm region inside the particle from the particle surface.

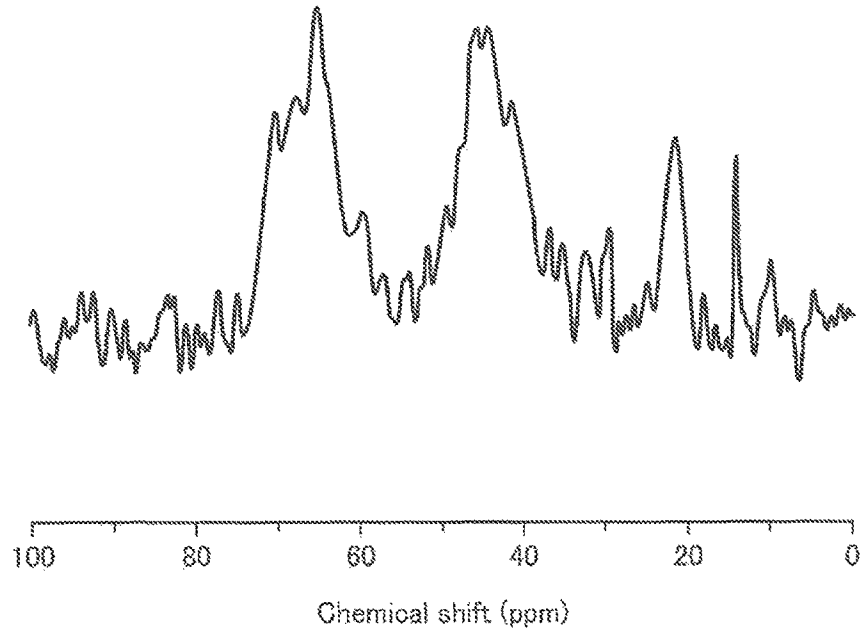
10 Claims, 3 Drawing Sheets

[Fig. 1]

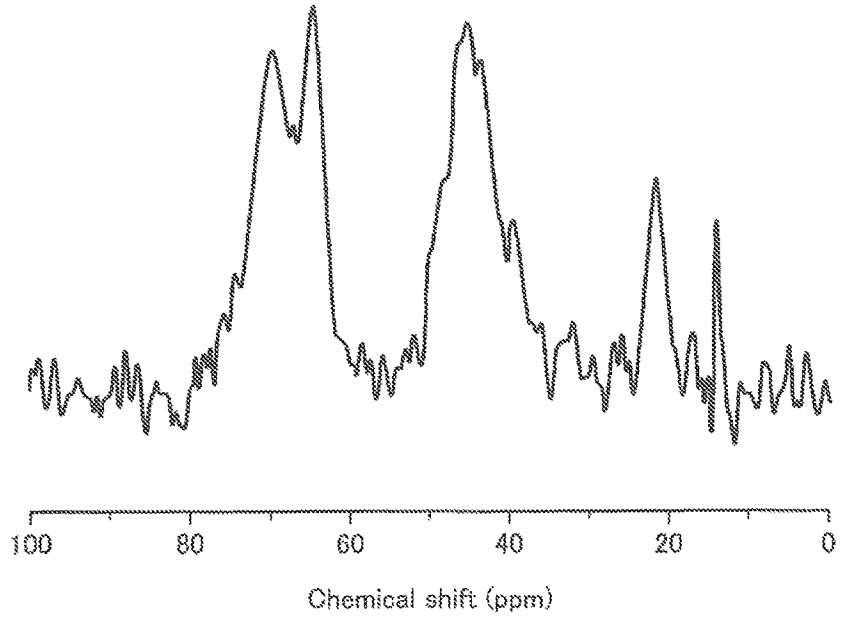


VACP : **Variable** Amplitude Cross Polarization
DD : Dipole Decoupling
PD : Post Delay
FID : Free Induction Decay

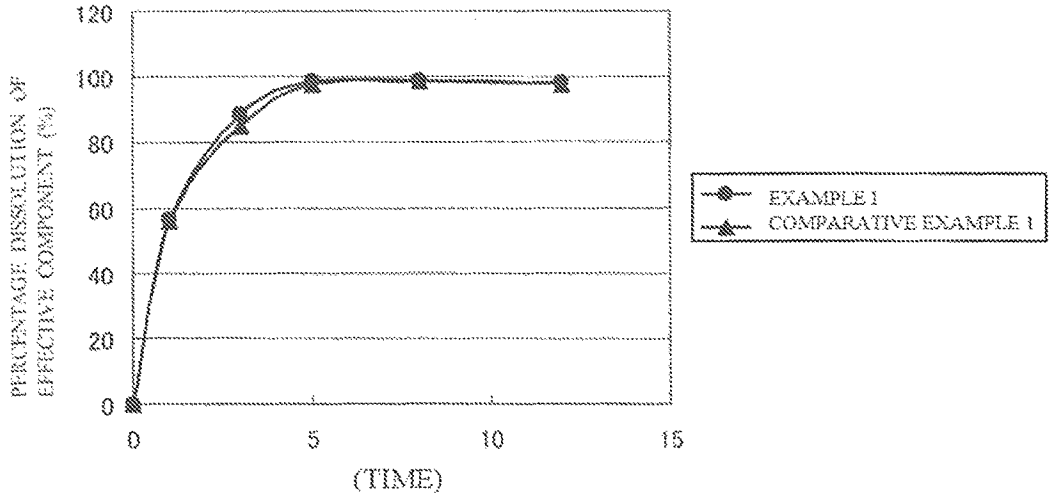
[Fig. 2]



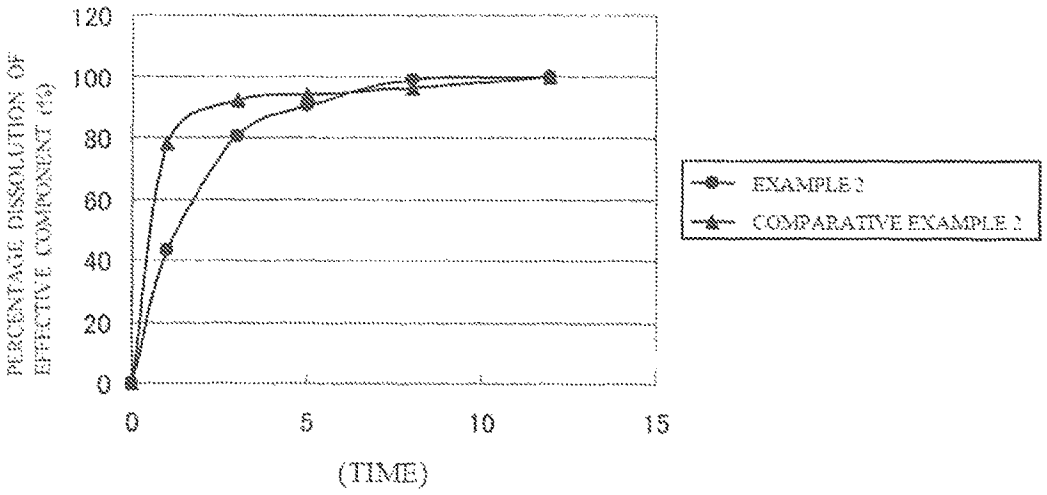
[Fig.3]


100
80
60
40
20
0
Chemical shift (ppm)

[Fig. 4]


120
100
80
60
40
20
0
0
5
10
15
(TIME)
PERCENTAGE DISSOLUTION OF EFFECTIVE COMPONENT (%)
EXAMPLE 1
COMPARATIVE EXAMPLE 1

[Fig. 5]


120
100
80
60
40
20
0
0
5
10
15
(TIME)
PERCENTAGE DISSOLUTION OF EFFECTIVE COMPONENT (%)
EXAMPLE 2
COMPARATIVE EXAMPLE 2

POLYVINYL ALCOHOL PARTICLES, PHARMACEUTICAL BINDER USING SAME, PHARMACEUTICAL TABLET, SUSTAINED-RELEASE PHARMACEUTICAL TABLET, AND METHOD FOR PRODUCING POLYVINYL ALCOHOL PARTICLES

TECHNICAL FIELD

The present invention relates to polyvinyl alcohol fine particles, pharmaceutical binders using same, pharmaceutical tablets, sustained-release pharmaceutical tablets, and a method for producing polyvinyl alcohol fine particles. Particularly, the invention relates to polyvinyl alcohol (hereinafter, also referred to simply as "PVA") fine particles that, when used as a pharmaceutical hinder, can produce pharmaceutical tablets of properties including good sustained release, high hardness, and excellent friability with a smooth surface. The invention also relates to pharmaceutical binders and pharmaceutical tablets consisting of the polyvinyl alcohol fine particles.

BACKGROUND ART

PVA is a water-soluble resin, and has been used in a wide range of applications by taking advantage of its characteristics. PVA is a powder or a granular solid in its product form, and widely used in various processes and applications typically after being dissolved in water.

Because of the conception that PVA is used after being dissolved in water, there are not many studies of PVA with regard to its characteristics in a product solid form.

However, a method that measures the surface condition of a film-like PVA is proposed recently. An analysis of a PVA film immersed in a non-solvent low-molecular liquid has revealed formation of larger numbers of intermolecular hydrogen bonds near the surface of PVA (see Non-Patent Document 1).

Use as an additive for pharmaceutical tablets is an example of PVA being directly used in solid form without being dissolved in water. Pharmaceutical tablet, a form of pharmaceutical preparations, is typically produced by tablet-forming. With respect to the method of tablet-forming, a granule obtained by granulating a powder mixture obtained by mixing various additive components with an effective ingredient (active ingredient) as a medicament, or the powder mixture is charged directly into a mortar, and molded into the desired size and shape by being compressed with pestle. The molded tablets are optionally coated with, for example, a cellulose compound or sugar, as required.

Examples of the additive components contained with the active ingredient in pharmaceutical tablets include: excipients (a component with no physiological activity, added to appropriately bulk up the formulation), binders (a component added to bind powder particles of raw materials, and to control the mechanical strength of the tablet), disintegrants (a component added to facilitate release of the active ingredient by disintegrating the tablet through expansion by absorbing moisture in the body), and lubricants (a component added to improve the fluidity of the powder for easy compression molding).

Among these additive components, the binder particularly has large impact on tablet strength. When the binder is not appropriately selected, there are problems such as molding failure, and tablet breaking occur after molding. The binder also affects the dissolution rate of active ingredient. Since the active ingredient is not easily absorbed if the tablet does not disintegrate when entering body, both the storage strength and the dissolution control upon administration are important and compatibility thereof is required. Particularly, sustained-release preparations, which are controlled to dissolve over a long time, have been actively developed since sustained-release preparations can improve the compliance by taking the medication less frequently, and, or prevent side effects by making the fluctuations of blood concentration smaller.

For example, Paten Document 1 discloses a binder using a polyvinyl alcohol copolymer of a specific average particle size. The binder is described as being most suitable for orally disintegrating tablets (OD tablets), and most suitable for direct tableting.

Patent Document 2 discloses that a polyvinyl alcohol copolymer is used for sustained-release preparations, and controlling dissolution over a long time is achieved by using it.

RELATED ART

Patent Document

Patent Document 1: JP-A-2013-087074
Patent Document 2: JP-A-2013-241341

Non-Patent Document

Non-Patent Document 1: T. Kanda and F. Horii., Proc. Soc. Solid State NMR Mater., No. 47, 43 (2010)

DISCLOSURE OF INVENTION

Technical Problem

The binder described in Patent Document 1 is suited for tableting, and can provide desirable immediate disintegrability for a tablet and release of active ingredient in a short time. While the binder is satisfactory in terms of above view points, it cannot control dissolution over a long time. The base material for matrix preparations described in Patent Document 2 is desirable in terms of sustained release of active ingredient, however, it is far from satisfactory in terms of the hardness and the friability of the obtained tablet. There accordingly is a need for a binder that has effect for both moldability and sustained release of a tablet.

Under these circumstances, the present invention is intended to provide PVA fine particles that, when used as a pharmaceutical binder in particular, can produce a pharmaceutical tablet of properties including good sustained release, high hardness, and excellent friability with a smooth surface. The invention is also intended to provide pharmaceutical binders, and pharmaceutical tablets.

Means for Solving the Problems

The present inventors conducted intensive studies to find a solution to the foregoing problems, and found that the problems can be solved with the use of polyvinyl alcohol fine particles having larger numbers of surface gauche structures than traditional polyvinyl alcohol fine particles. The present invention was completed on the basis of this finding.

Specifically, the present invention has the following configurations (1) to (11).

(1) A polyvinyl alcohol fine particle, comprising: 25 mol % or more of a gauche structure in polyvinyl alcohol molecules within a 0.8-nm region inside the particle from the particle surface.

(2) The polyvinyl alcohol fine particle according to (1), wherein the ratio (S1/S2) of an average degree of saponification (S1) of the polyvinyl alcohol fine particle to an average degree of surface saponification (S2) in the 0.8-nm region inside the particle from the particle surface is 1.10 or more.

(3) The polyvinyl alcohol fine particle according to (1) or (2), which is obtainable by pulverizing a dry powder of an unmodified polyvinyl alcohol consisting of solely a vinyl alcohol structure unit and a vinyl ester structure unit.

(4) The polyvinyl alcohol fine particle according to (3), wherein a 50% particle size of the dry powder of the unmodified polyvinyl alcohol is 50 to 2,000 μm.

(5) The polyvinyl alcohol fine particle according to any one of (1) to (4), wherein a 50% particle size of the polyvinyl alcohol fine particle is 1 to 200 μm.

(6) The polyvinyl alcohol fine particle according to any one of (1) to (5), which has an average degree of polymerization of 200 to 4,000.

(7) The polyvinyl alcohol fine particle according to any one of (1) to (6), comprising: an alkali metal salt in an amount of 0.001 to 2 mass % of the polyvinyl alcohol fine particle.

(8) A pharmaceutical binder, comprising: the polyvinyl alcohol fine particle of any one of (1) to 7).

(9) A pharmaceutical tablet, comprising: an active ingredient; and the pharmaceutical binder of (8).

(10) A sustained-release pharmaceutical tablet, comprising: an active ingredient; and the pharmaceutical hinder of (8).

(11) A method for producing a polyvinyl alcohol fine particle, comprising: washing and drying an unmodified polyvinyl alcohol obtained from a vinyl alcohol structure unit; and a vinyl ester structure unit, and pulverizing an obtained dry powder of the unmodified polyvinyl alcohol.

Advantageous Effects of Invention

The pharmaceutical binder of PVA fine particles of the present invention has large numbers of surface gauche structures, and this is believed to reduce surface crystallinity, and increase adhesion. A pharmaceutical tablet using the pharmaceutical binder of the present invention thus has properties including good sustained release, high hardness, and excellent friability, and the tableting surface condition is smooth.

The detailed mechanism by which large numbers of surface gauche structures provide the effects of the present invention remains unclear. However, considering that the gauche structure is a disrupted crystalline structure, the improved adhesion appears to be due to the disrupted crystalline structure on the surface of PVA fine particles. It is believed that the properties of the pharmaceutical tablet, including good sustained release, high hardness, and excellent friability with a smooth surface condition when tableting, are the result of the improved adhesion,

BRIEF DESCRIPTION OF DRAWINGS

FIG. **1** is a diagram representing a pulse sequence used for NMR measurements performed in the present invention.

FIG. **2** shows a solid-state NMR chart of Examples 1 and 2.

FIG. **3** shows a solid-state NMR chart of Comparative Examples 1 and 2.

FIG. **4** is a diagram representing the percentage dissolution of active ingredient of Example 1 and Comparative Example 1.

FIG. **5** is a diagram representing the percentage dissolution of active ingredient of Example 2 and Comparative Example 2.

EMBODIMENTS FOR CARRYING OUT THE INVENTION

The present invention is described below in detail. As used herein, percent and part used with mass have the same meaning as percent or part by weight.

PVA Fine Particles

The PVA fine particles of the present invention includes a polyvinyl alcohol (hereinafter, also referred to simply as "PVA") having a vinyl alcohol structure unit, and a vinyl ester structure unit representing an unsaponified moiety. The PVA fine particles contain 25 mol % or more of a gauche structure in PVA molecules within a 0.8-nm region inside the PVA fine particles from the particle surface.

Preferably, with respect to f the PVA fine particles, the ratio (S1/S2) of the average degree of saponification (S1) to the average degree of surface saponification (S2) in a 0.8-nm region inside the particles from the particle surface is 1.10 or more.

A gauche structure refers to a torsional structure of a carbon-carbon bond in the main chain of PVA. A structure without torsion is planar, and is called a trans structure. Typically, a carbon-carbon bond in the main chain of PVA has either a gauche structure or a trans structure, and most of the carbon-carbon bonds have a trans structure.

A gauche structure results when a trans structure is rotated 60°. Because of the torsion, the crystallinity and the amount of hydrogen bond in the PVA molecules tend to decrease as the number of gauche structures increases.

The PVA fine particles of the present invention contain 25 mol % or more, preferably 27 mol % or more, particularly preferably 30 to 50 mol % of a gauche structure in PVA molecules in a 0.8-nm region inside the PVA fine particles from the particle surface.

There is a tendency that the effects of the present invention is hard to be obtained when this rate is too small.

The PVA fine particles containing 25 mol % or more of a gauche structure in PVA molecules within a 0.8-nm region inside the particles from the particle surface can be obtained by, for example, heating the PVA fine particle surface, pulverizing the PVA particles via collision, or washing the PVA fine particles with a solvent that does not dissolve PVA. These methods may be used in combination.

Among these, it is preferable that the PVA fine particles are washed with a solvent that does not dissolve PVA, dried, and pulverized via collision.

In the PVA fine particles of the present invention, the ratio (S1/S2) of the average degree of saponification (S1) of the whole particles to the average degree of surface saponification (52) in a 0.8-nm region inside the particles from the particle surface is preferably 1.10 or more, more preferably 1.10 to 1.50. There is a tendency that the effects of the present invention is hard to be obtained when this ratio is too small.

The PVA fine particles satisfying the ratio can be obtained by, for example, heating the PVA fine particle surface, pulverizing the PVA particles via collision, or washing the

PVA fine particles with a solvent that does not dissolve PVA. These methods may be used in combination.

Among these, it is preferable that the PVA fine particles are washed with a solvent that does not dissolve PVA, dried, and pulverized via collision.

The following specifically describes the methods for measuring the gauche structure, and the average degree of surface saponification (S2). The methods for measuring are based on the techniques described in JP-A-2008-203159, and in T. Randa and F. Horii., Proc. Soc. Solid State NMR Mater., No. 47, 43 (2010).

High-resolution solid-state NMR is used for structure analysis. The pulse sequence shown in FIG. **1** is used for measurement. Each of the parameters by used this is presented in Table 1 below. n-Decane is added in the same amount as the mass of the polyvinyl alcohol fine particles charged into a zirconia rotor having a diameter ϕ of 4 mm which is a sample tube.

TABLE 1

Measurement conditions

Device Probe	Braker AVANCEIII 400WB CP/MAS probe (ϕ = 4 mm)
Temperature	Room temperature (22° C.)
Medium	n-decane
Observed nucleus	^{13}C
Rotation of sample tube	5,000 Hz
^{1}H 90° pulse	4.2 μs
Contact time	350 μs
τt	72 μs
τd	1 ms, 20 ms, 50 ms, 100 ms
FID signal capture time	14 ms
Runs	>3,000
Observation center	120 ppm
Observation range	365 ppm
Waiting time	20 s

In Table 1, τt represents a portion due to the ^{1}H nucleus spin-spin relaxation of n-decane which is the polyvinyl alcohol fine particles and the medium. The magnetization of the polyvinyl alcohol fine particles cancels out with a τt of 60 μs or longer, whereas the magnetization of the n-decane remains to provide a condition for spin diffusion.

Increasing the τd time enhances the resonance line of a spectrum, and it is observed that spin diffusion occurs.

With the spin diffusion, the magnetization from the n-decane permeates into the polyvinyl alcohol fine particles through the particle surface. The spin diffusion time can be represented by a distance function of the formula (1) below. A spectrum obtained from a very short spin diffusion time represents a structure with a short distance L (nm) from the PVA fine particle surface into the particle, specifically a structure in the vicinity of the surface.

$$L=(a\times D\times \tau d)^{0.5} \quad (1)$$

(In formula (1), a is a constant with the value 4/3, the diffusion constant D has an assumed value of 0.5 nm/ms, and τd represents the spin diffusion time (ms).)

It is to be noted that the constants a and D are described in K. Masuda, M. Adachi, H. Yamamoto, H. Koji, and F. Horii, Solid State NMR, 23, 198 (2003), and in J. R. Havens and D. L. VanderHart, Macromolecules, 23, 1663 (1985).

Solving the equation (1) for L by substituting the constants with the foregoing numbers and the τd with the minimum value, 1, of spin diffusion time (ms) yields a value of 0.8 nm as the distance from the PVA fine particle surface into the particle when an effective value of is the first decimal place. The number is the least measurable value, and represents a distance corresponding to a single molecule of PVA.

The peaks in the obtained spectrum are separated at 46 ppm (CH_2 with a trans-trans structure in the main chain of polyvinyl alcohol), 41 ppm (CH_2 with a trans-gauche structure in the main chain of polyvinyl alcohol), 36 ppm (CH_2 with a gauche-gauche structure in the main chain of polyvinyl alcohol), and 21 ppm (CH_3 in the residual acetyl of polyvinyl alcohol), using a Gaussian function. The area of each peak is then calculated.

The content of the gauche structure in the PVA molecules residing in a 0.8-nm region inside the particles from the particle surface is calculated according to the following formula (2).

$$\text{Gauche structure (mol \%)}=100\times(B/2+C)/(A+B+C) \quad (2)$$

(In formula (2), A represents the peak area at 46 ppm, B represents the peak area at 41 ppm, and C represents the peak area at 36 ppm.)

The degree of surface saponification is calculated according the following formula (3).

$$\text{Degree of saponification (mol \%)}=100\times(1-D/(A+B+C)) \quad (3)$$

(In formula (3), A represents the peak area at 46 ppm, B represents the peak area at 41 ppm, C represents the peak area at 36 ppm, and D the peak area at 21 ppm.)

The following re specifically describes the method of production of PVA fine particles.

The PVA which is a feedstock of PVA fine particles may be obtained through saponification of, for example, a polyvinyl ester polymer polymerized from vinyl ester monomers.

Examples of the vinyl ester monomers include vinyl formate, vinyl acetate, vinyl propionate, vinyl valerate, vinyl butyrate, vinyl isobutyrate, vinyl pivalate, vinyl caprate, vinyl laurate, vinyl stearate, vinyl benzoate, and vinyl versatate. Preferred for practicality is vinyl acetate.

It is also possible to use saponification products of copolymers of the vinyl ester monomers and monomers that are copolymerizable with the vinyl ester monomers, provided that such copolymers do not inhibit the effects of the present invention. Examples of such copolymerizable monomers include:

olefins such as ethylene, propylene, isobutylene, α-octene, α-dodecene, and α-octadecene;

hydroxyl-containing α-olefins such as 3-buten-1-ol, 4-penten-1-ol, 5-hexen-3,4-dihydroxy-1-butene, and derivatives thereof such as acylates;

unsaturated acids such as acrylic acid, methacrylic acid, crotonic acid, maleic acid, a maleic acid anhydride, itaconic acid, and undecylenic acid, and salts, monoesters, and dialkyl esters thereof;

nitriles such as acrylonitrile, and methacrylonitrile;

amides such as diacetoneacrylamide, acrylamide, and methacrylamide;

olefin sulfonic acids such as ethylene sulfonic acid, allyl sulfonic acid, methallyl sulfonic acid, and salts thereof;

vinyl compounds such as alkyl vinyl ethers, dimethylallyl vinyl ketone, N-vinyl pyrrolidone, vinyl chloride, vinyl ethylene carbonate, 2,2-dialkyl-4-vinyl-1,3-dioxolan, and glycerine monoallyl ether;

substituted vinyl acetates such as isopropenyl acetate, and 1-methoxy vinyl acetate;

vinylidene chloride, 1,4-diacetoxy-2-butene, 1,4-dihydroxy-2-butene, and vinylene carbonate.

The content of the copolymerizable monomer is typically 10 mol % or less, preferably 5 mol % or less, particularly preferably 1 mol % or less with respect to the total polymer amount. In the present invention, the PVA is preferably an unmodified PVA of solely a vinyl alcohol structure unit, and a vinyl ester structure unit representing an unsaponified moiety.

The method of polymerization of the vinyl ester monomer and the copolymerizable monomer is not particularly limited, and known methods such as bulk polymerization, solution polymerization, suspension polymerization, dispersion polymerization, and emulsion polymerization may be used. Typically, solution polymerization is used.

Typical examples of the solvent used for the polymerization include aliphatic alcohols of 1 to 4 carbon atoms such as methanol, ethanol, isopropyl alcohol, n-propanol, and butanol, and ketones such as acetone, and methyl ethyl ketone. Preferred for industrial applications is methanol.

The polymerization reaction is performed with known radical polymerization catalysts such as azobisisobutyronitrile, acetyl peroxide, benzoyl peroxide, and lauroyl peroxide, or various known cold activation catalysts. The reaction temperature is selected from a range of from about 35° C. to the boiling point.

The polyvinyl ester polymer is saponified either continuously or in a batch. The saponification may be alkali saponification or acid saponification. In industrial applications, the polymer is dissolved in alcohol, and saponified in the presence of an alkali catalyst. Examples of the alcohol include methanol, ethanol, and butanol. The polymer concentration in alcohol is selected from a range of from 20 to 60 mass %. About 0.3 to 10 mass % of water may be added, as required. It is also possible to add various solvents, for example, such as esters (e.g., methyl acetate), benzene, hexane, and DMSO (dimethylsulfoxide).

Specific examples of the saponification catalyst include alkali catalysts, for example, such as hydroxides of alkyl metals (e.g., sodium hydroxide, potassium hydroxide, sodium methylate, sodium ethylate, and potassium methylate), and alcoholate. Preferably, the catalyst is used in a 1 to 100 millimolar equivalent with respect to the monomer.

After saponification, the obtained polyvinyl ester polymer is washed with a washing liquid. Examples of the washing liquid include alcohols such as methanol, ethanol, isopropyl alcohol, and butanol. Preferred for washing efficiency and drying efficiency is methanol.

The washing may be performed continuously (e.g., rotational washing with a cylinder, counterflow contact washing, and centrifugal spray washing). However, batch washing is typically employed. The stirring method (stirring device) used for washing may be, for example, a screw blade, a ribbon blender, or a kneader. The bath ratio (mass of washing liquid/mass of polyvinyl ester polymer particles) is typically 1 to 30, particularly preferably 2 to 20. A large washing device will be required, and the cost tends to increases when the bath ratio is excessively large. An excessively small bath ratio often leads to poor washing performance, and frequent washing.

The washing temperature is typically 10 to 80° C., particularly preferably 20 to 70° C. An excessively high temperature tends to increase the vaporization of the washing liquid, and necessitate reflux equipment. The washing efficiency tends to decrease when the temperature is too low. The washing time is typically 5 minutes to 12 hours, particularly preferably 30 minutes to 4 hours. An excessively long washing time tends to cause poor production efficiency, whereas insufficient washing tends to result when the washing time is too short. The washing is performed typically 1 to 10 times, particularly preferably 1 to 5 times. Productivity suffers, and the cost tends to increase when washing is performed too frequently.

The washed polyvinyl ester polymer particles are dried with, for example, hot air, either continuously or in a hatch, to obtain a PVA powder. The drying temperature is typically 50 to 150° C., preferably 60 to 130° C., further preferably 70 to 110° C. An excessively high drying temperature tends to cause heat deterioration of the polyvinyl ester polymer particles, whereas the drying often takes a long time when the drying temperature is too low. The drying time is typically 1 to 48 hours, particularly preferably 2 to 36 hours. An excessively long drying time tends to cause heat deterioration of the polyvinyl ester polymer particles, whereas an excessively short drying time tends to cause insufficient drying, or necessitate high-temperature drying.

The content of the solvent in the dried unmodified PVA powder is typically 0 to 10 mass %, preferably 0.1 to 5 mass %, and further preferably 0.1 to 1 mass %.

The unmodified PVA powder contains an alkali metal salt of acetic acid originating in the alkali catalyst used for saponification. The content of the alkali metal salt is typically 0.001 to 2 mass %, preferably 0.005 to 1 mass %, further preferably 0.01 to 0.1 mass % with respect to the unmodified PVA powder.

The content of the alkali metal salt may be adjusted by, for example, adjusting the amount of the alkali catalyst used for saponification, or by washing the PVA with alcohols such as ethanol and methanol.

In the present invention, the alkali metal salt may be quantified by, for example, dissolving the PVA powder in water, and determining the content through neutralization titration with hydrochloric acid, using methyl orange as an indicator.

The PVA used in the present invention has an average degree of polymerization of preferably 200 to 4,000, more preferably 400 to 3,500, further preferably 500 to 3,000. When the average degree of polymerization is too small, it may not be possible to obtain sufficient adhesion or sustained release in the tablet. On the other hand, moldability may suffer when the average degree of polymerization is too large, as it makes it difficult to mix the PVA with other components such as an active ingredient, and an excipient. In the present invention, the average degree of polymerization is a measured value according to the JIS K6726 method.

The viscosity of a 4 mass % aqueous solution of PVA at 20° C. is preferably 1.5 to 100 mPa·s, more preferably 4 to 80 mPa·s, further preferably 5 to 70 mPa·s. When the viscosity of the 4 mass % aqueous solution is too large, moldability may suffer as the solvent causes gelation, makes mixing difficult during production. On the other hand, sufficient adhesion or sustained release may not be obtained when the viscosity of the 4 mass % aqueous solution is too small. In the present invention, the viscosity of the 4 mass % aqueous solution at 20° C. is a measured value according to the JIS K6726 method.

The PVA used in the present invention has a degree of saponification of preferably 70 to 100 mol %, more preferably 80 to 95 mol %, further preferably 85 to 90%. When the degree of saponification is too low, it may not be possible to maintain sustained release. When the degree of saponification is too high, quick disintegration may occur due to the lack of adhesion. In the present invention, the degree of saponification is a measured value according to the JIS K6726 method.

Typically, the predominant form of bonding in the main chain of PVA is the 1,3-diol linkage, and the 1,2-diol linkage accounts for only about 1.5 to 1.7 mol %. However, the PVA used in the present invention may be one in which the 1,2-diol linkage has been increased to 1.7 to 3.5 mol % by increasing the polymerization temperature of the polymerization of the vinyl ester monomer.

In the present invention, the unmodified PVA powder after drying and before pulverization has a 50% particle size of preferably 50 to 2,000 μm, more preferably 60 to 1,500 μm, further preferably 70 to 1,000 μm. Handling in the washing or pulverization of PVA may suffer when the 50% particle size of the unmodified PVA powder is too small. On the other hand, washing efficiency and pulverization efficiency may suffer when the 50% particle size of the unmodified PVA powder is too large. The 50% particle size is the diameter at 50% in the cumulative value (cumulative distribution) obtained from the measured laser diffraction volume distribution by particle size.

It is particularly preferable in the present invention to pulverize the PVA dry powder into PVA fine particles as the pharmaceutical binder of the present invention.

Conceivably, the surface of the PVA dry powder undergoes changes due to external factors such as washing and drying in the production of the unmodified PVA dry powder.

The unmodified PVA dry powder is pulverized to expose the inside and to be the PVA fine particles that have undergone surface changes. A tablet produced by adding the PVA fine particles as a pharmaceutical binder can have improvement in hardness, moldability, and sustained release.

In the pulverization step, the PVA powder is pulverized into the desired particle size to obtain the PVA fine particles of the present invention. From the standpoint of the moldability, surface smoothness, and sustained release of the tablet, the 50% particle size of the PVA fine particles is preferably 1 to 200 μm, more preferably 10 to 180 μm, further preferably 15 to 150 μm. When the 50% particle size of the pulverized PVA fine particles is too small, the powder mixture cannot have desirable fluidity, and it often becomes difficult to produce a uniform preparation. When the 50% particle size of the pulverized PVA fine particles is too large, the surface area becomes smaller, and the adhesion and sustained release tend to suffer.

The PVA fine particles have the same average degree of polymerization as the PVA before pulverization. Specifically, the PVA fine particles has an average degree of polymerization of preferably 200 to 4,000, more preferably 400 to 3,500, further preferably 500 to 3,000. When the average degree of polymerization is too small, the tablet may fail to have sufficient adhesion and sustained release. On the other hand, moldability may suffer when the average degree of polymerization is too large, as it makes it difficult to mix the PVA fine particles with other components such as an active ingredient, and an excipient.

The method for pulverizing the PVA dry powder is not particularly limited, and the PVA dry powder may be pulverized by using, for example, a roller mill, a bead mill, a ball mill, a jet mill, a hammer mill, or a pin mill, or by grinding pulverization or collision pulverization. A method using collision pulverization is preferred because it involves only limited heat on the obtained PVA fine particles. Parameters such as pulverization temperature and pulverization time may be appropriately set according to the means of pulverization, as long as the desired particle size is obtained.

For example, collision pulverization is a method that pulverizes the PVA dry powder via self collision in a high-speed swirling airflow. This method is preferred in the present invention because it involves only small air friction and small temperature increase, and reduces heat deterioration of the PVA fine particles with the reduced abrasion.

In the pulverization method using collision pulverization, the pulverization temperature is preferably 10 to 100° C., more preferably 20 to 80° C.

The PVA fine particles of the present invention obtained in the manner described above can preferably be used as a pharmaceutical binder used as an additive of pharmaceutical tablets.

Active Ingredient

Examples of the active ingredients used in the present invention include antipyretic analgesic antiphlogistics, nutrient and tonic supplements, psychotropics, antidepressants, antianxiety drugs, hypnosedatives, anticonvulsants, CNS-acting drugs, brain metabolism improving agents, brain circulation improving agents, antiepileptic agents, sympathomimetic drugs, gastrointestinal drugs, acid suppressants, anti-ulcerogenic drugs, cough medicines, antiemetics, anapnoics, bronchodilators, allergic drugs, antihistamine agents, agents for dental and oral use, cardiants, agents for cardiac arrhythmia, diuretics, hypertension drugs, vasoconstrictors, coronary vasodilators, peripheral vasodilators, blood coagulation inhibitors, hyperlipidemias agents, cholagogues, antibiotics, chemotherapeutic agents, diabetes drugs, osteoporosis drugs, antirheumatics, skeletal muscle relaxants, antispasmodics, hormonal agents, alkaloid drugs, sulfa drugs, arthrifuges, and antineoplastics.

Examples of the antipyretic analgesic antiphlogistics include acetaminophen, aspirin, ibuprofen, ethenzamide, diphenhydramine hydrochloride, dl-chlorpheniramine maleate, diclofenac sodium, dihydrocodeine phosphate, salicylamide, aminopyrine, noscapine, methylephedrine hydrochloride, phenylpropanolamine hydrochloride, serrapeptase, lysozyme chloride, tolfenamic acid, mefenamic acid, flufenamic acid, ketoprofen, indometacin, bucolome, pentazocine, caffeine, and anhydrous caffeine.

Examples of the nutrient and tonic supplements include vitamins such as vitamin A, vitamin B1 (e.g., dibenzoylthiamine, and fursulthiamine hydrochloride), vitamin B2 (e.g., riboflavin butyrate), vitamin B6 (e.g., pyridoxine hydrochloride), vitamin B12 (e.g., hydroxocobalamin acetate, and cyanocobalamin), vitamin C (e.g., ascorbic acid, and sodium L-ascorbate), vitamin D, and vitamin E (e.g., d-α-tocopherol acetate); minerals such as calcium, magnesium, and iron; proteins, amino acids, oligosaccharides, and crude drugs.

Examples of the psychotropics include chlorpromazine, and reserpine.

Examples of the antidepressants include amphetamine, imipramine, and maprotiline hydrochloride.

Examples of the antianxiety drugs include diazepam, alprazolam, and chlordiazepoxide.

Examples of the hypnosedatives include estazolam, diazepam, nitrazepam, perlapine, and phenobarbital sodium.

Examples of the anticonvulsants include scopolamine hydrobromide, diphenhydramine hydrochloride, and papaverine hydrochloride.

Examples of the CNS-acting drugs include citicoline.

Examples of the brain metabolism improving agents include meclofenoxate hydrochloride.

Examples of the brain circulation improving agents include vinpocetine.

Examples of the antiepileptic agents include phenitoin, and carbamazepine.

Examples of the sympathomimetic drugs include isoproterenol hydrochloride.

Examples of the gastrointestinal drugs include stomach digestive aids such as diastase, saccharated pepsin, a scopolia extract, cellulase AP3, lipase AP, and cinnamon oil; and antiflatulents such as berberine chloride, resistant lactic acid bacteria, and bifidobacteria.

Examples of the acid suppressants include magnesium carbonate, sodium bicarbonate, magnesium aluminometasilicate, synthetic hydrotalcite, precipitated calcium carbonate, and magnesium oxide.

Examples of the anti-ulcerogenic drugs include lansoprazole, omeprazole, rabeprazole, cimetidine, famotidine, and ranitidine hydrochloride.

Examples of the cough medicines include cloperastine hydrochloride, dextromethorphan hydrobromide, theophylline, guaiacol potassium sulfonate, gualfenesin, and codeine phosphate.

Examples of the antiemetics include difenidol hydrochloride, and metoclopramide.

Examples of the anapnoics include levallorphan tartrate.

Examples of the bronchodilators include theophylline, and sulbutamol sulfate.

Examples of the allergic drugs include amlexanox, and seratrodast.

Examples of the antihistamine agents include diphenhydramine hydrochloride, promethazine, isothipendyl hydrochloride, and dl-chlorpheniramine maleate.

Examples of the agents for dental and oral use include oxytetracycline, triamcinolone acetonide, chlorhexidine hydrochloride, and lidocaine.

Examples of the cardiants include digoxin, and caffeine.

Examples of the agents for cardiac arrhythmia include procainamide hydrochloride, propranolol hydrochloride, and pindolol.

Examples of the diuretics include furosemide, isosorbide, and hydrochlorothiazide.

Examples of the hypertension drugs include captopril, delapril hydrochloride, hydralazine hydrochloride, labetalol hydrochloride, manidipine hydrochloride, candesartan cilexetil, methyldopa, and perindopril erbumine.

Examples of the vasoconstrictors include phenylephrine hydrochloride.

Examples of the coronary vasodilators include carbocromen hydrochloride, molsidomine, and verapamil hydrochloride.

Examples of the peripheral vasodilators include cinnarizine.

Examples of the blood coagulation inhibitors include dicumarol.

Examples of the hyperlipidmias agents include cerivastatin sodium, simvastatin, pravastatin sodium, and an atorvastatin calcium hydrate.

Examples of the cholagogues include dehydrocholic acid, and trepibutone.

Examples of the antibiotics include cephem antibiotics such as cephalexin, amoxicillin, cefaclor, pivmecillinam hydrochloride, cefotiam hexetil hydrochloride, cephadroxil, cefixime, cefditoren pivoxil, cefteram pivoxil, and cefpodoxime proxetil; monobactam antibiotics such as synthetic anti-microbial agent carumonam sodium, including ampicillin, ciclacillin, nalidixic acid, and enoxacin; and penem and carbapenem antibiotics.

Examples of the chemotherapeutic agents include sulfamethizole.

Examples of the diabetes drugs include glymidine sodium, glipizide, phenformin hydrochloride, buformin hydrochloride, metformin, metfomin hydrochloride, tolbutamide, voglibose, pioglitazone hydrochloride, glibenclamide, and troglitazone.

Examples of the osteoporosis drugs include ipriflavone.

Examples of the skeletal muscle relaxants include methocarbamol.

Examples of the antispasmodics include meclizine hydrochloride, and dimenhydrinate.

Examples of the antirheumatics include methotrexate, and bucillamine.

Examples of the hormonal agents include liothyronine sodium, dexamethasone sodium phosphate, prednisolone, oxendolone, and leuprorelin acetate.

Examples of the alkaloid drugs include opium, morphine hydrochloride, ipecacuanha, oxycodone hydrochloride, opium alkaloids hydrochlorides, and cocaine hydrochloride.

Examples of the sulfa drugs include sulfisomidin, and sulfamethizole.

Examples of the arthrifuges include allopurinol, and colchicine.

Examples of the antineoplastics include 5-fluorouracil, uracil, and mitomycin.

The content of the active component is appropriately adjusted according to bioavailability. The active component may be diluted with diluents commonly used in the field of medicine and food. The active component may be one that has been treated to mask bitterness.

Other Additives

Various additives may be added to the pharmaceutical tablet of the present invention, provided that it is not detrimental to the effects of the present invention. Examples of such additives include excipients, disintegrants, pH adjusters, fluidizers, surfactants, colorants, sweeteners, and coating agents.

The excipient may be one or two or more components selected from, for example, sugar alcohols, sugars, calcium phosphate, crystalline cellulose, starch, sodium phosphate, and gelatin. The preferred excipients are sugar alcohols, and sugars.

Examples of the sugar alcohols include mannitol, erythritol, xylitol, sorbitol, and maltitol. Examples of the sugars include glucose, fructose, lactose, sucrose, trehalose, maltose, and oligosaccharides.

Examples of the disintegrants include carmellose calcium, carboxymethyl starch sodium, croscarmellose sodium, crospovidone, celluloses and derivatives thereof, and starches and derivatives thereof.

Examples of the pH adjusters include citric acid and salts thereof, phosphoric acid and salts thereof, carbonic acid and salts thereof, tartaric acid and salts thereof, fumaric acid and salts thereof, acetic acid and salts thereof, amino acids and salts thereof, succinic acid and salts thereof, and lactic acid and salts thereof.

Examples of the fluidizers include, light anhydrous silicic acid, hydrous silicon dioxide, titanium oxide, stearic acid, a corn gel, and a heavy anhydrous silicic acid.

Examples of the surfactants include phospholipids, glycerin fatty acid esters, polyoxyethylene fatty acid esters, sorbitan fatty acid esters, polyethylene glycol fatty acid esters, polyoxyethylene hydrogenated castor oil, polyoxyethylene alkyl ethers, sucrose fatty acid esters, sodium lauryl sulfate, polysorbates, sodium hydrogen phosphates, and potassium hydrogen phosphates.

Examples of the colorants include iron sesquioxide, yellow iron sesquioxide, food yellow 5, food yellow 4, aluminum chelate, titanium oxide, and talc.

Examples of the sweeteners include saccharin, aspartame, acesulfame potassium, thaurnatin, and sucralose.

Examples of the coating agents include hydroxypropyl cellulose, hydroxypropyl methylcellulose, methylcellulose, polyvinyl alcohol, polyvinylpyrrolidone-ethyl acrylate, a methyl methacrylate copolymer dispersion, hydroxypropyl methylcellulose acetate succinate, and a methacrylic acid copolymer.

Pharmaceutical Tablet

The pharmaceutical tablet of the present invention is produced by mixing the foregoing components, followed by tablet compression, either directly or after being granulated.

The molding may be performed by using any of the methods commonly used for the compression molding of solid preparations in the field of medical drug products, including methods using a rotary tableting machine, and methods using a single-press tableting machine. For example, the pharmaceutical tablet of the present invention may be produced by using a direct powder compression method in which the components are compressed after being uniformly mixed, or a wet or dry granulation compression method in which the components are compressed as granules after being granulated by a wet or dry method.

Preferred for improved fluidity and mixture uniformity is the wet granulation compression method.

The wet granulation method is not particularly limited, as long as the components are granulated. The wet granulation method may be appropriately selected from known methods according to the intended use. Examples of such methods include wet disintegration, extrusion, a fluidized bed, and stirring. Among these, preferably, the wet granulation method is, for example, a stirring granulation method, or a fluidized bed granulation method, more preferably the stirring granulation method.

The device used for granulation is not particularly limited, and may be appropriately selected according to the intended use. Examples of the granulation device include a stirring granulation device (for example, Rapid Mixer Granulator available from Gem Pharma Machineries, and Vertical Granulator available from Powrex Corporation), and a fluidized bed granulation device (for example, a tumbling fluidized coating device MP-01 available from Powrex Corporation).

In the granulation step, the components are weighed, sieved and pulverized, and mixed in a granulator in a dry state. For granulation, it is preferable to add water or a solvent, or a mixture of water and a solvent to the powder mixture. The solvent may be appropriately selected according to the properties of the effective ingredient. Examples of the solvent include alcohols such as ethanol, butanol, and isopropyl alcohol. Preferred is isopropyl alcohol.

The granulated material is then subjected to tablet compression. The tablet compression may be performed by using various tableting machines, for example, such as the model HT-APSS, HT-AP-MS, HT-X-SS, and HT-X-MS available from Hata Tekkosho Co., Ltd., and VIRGO, AQUARIUS, and LIBRA available from Kikusui Seisakusho.

The pharmaceutical tablet may have any shape, including an ellipsoid, a column, a doughnut, and a sphere.

EXAMPLES

The following describes the present invention in greater detail with reference to Examples. However, the present invention is not limited to the following Examples, as long as the gist of the present invention does not depart from the following descriptions.

In the following, "part" means "part by mass."

A polyvinyl (PVA) alcohol polymer was prepared, and tablets were produced from an unmodified polyvinyl alcohol obtained by saponifying the obtained PVA polymer, as follows. The PVA polymer was measured for degree of saponification, and 4 mass % aqueous solution viscosity. The tablets were measured for hardness, and evaluated for friability and sustained release. The measurements were performed according to the following methods.

Degree of Saponification

Degree of saponification was measured according to the JIS K6726 method.

4 Mass % Aqueous Solution Viscosity

4 Mass % aqueous solution viscosity was measured according to the JIS K6726 method.

Hardness Evaluation

Hardness was evaluated with a Monsanto hardness tester.

Friability Evaluation

The tablet was placed in a tablet friability apparatus (available from Electrolab, India), and the drum was rotated at 25 rpm for 4 min. The mass of the tablet was then measured outside of the drum. The tablet friability was calculated as follows. In the equation, "mass loss" is obtained by subtracting the tablet mass after the testing from the initial tablet mass.

$$\text{Percent Friability} = (\text{mass loss}/\text{initial tablet mass}) \times 100$$

Sustained Release

Suitability as a pharmaceutical tablet was evaluated after stirring the tablet in 900 mL of phosphate buffer (pH 6.8) at 50 rpm at 37±0.5° C., using a Dissolution Apparatus Type I (TDT-08L available from Electrolab, India). The solution (5 ml) was sampled at certain time intervals, and the amount of metformin hydrochloride that had dissolved out of the tablet was measured at 233 nm, using a UV spectrophotometer (V-530 available from Jasco).

Tablet Shape

The shape of the molded tablet was visually inspected, and evaluated according to the following criteria.

Smooth: The tablet surface was smooth and did not discharge powders

Rough: The tablet surface had a rough texture and discharge powders

Example 1

Production of Polyvinyl Alcohol

1,000 Parts of vinyl acetate, 140 parts of methanol, and 0.05 mol % of azobisisobutyronitrile (relative to the vinyl acetate) were charged into a reaction vessel equipped with a reflux condenser, a dripping funnel, and an agitator. Heat was applied while stirring the mixture under a stream of nitrogen to allow polymerization for 5 hours below the boiling point. m-Dinitrobenzene was added to quench the polymerization upon completion of polymerization of 65% of the vinyl acetate, and the unreacted vinyl acetate monomers were removed out of the system under injected methanol steam to obtain a methanol solution of PVA polymer (resin content of 41%).

The methanol solution was furthermore diluted with methanol, and charged into a kneader after adjusting the concentration to 33%. At the maintained solution temperature of 40° C., a 3.5% methanol solution of sodium hydroxide was added in a proportion of 2.0 millimoles per mole of the vinyl acetate structure unit in the polymer to initiate saponification. A saponified product that precipitated out of

the solution and formed particles in the course of saponification was filtered by solid-liquid separation.

The PVA dry powder had a degree of saponification of 87.7 mol % as measured by an analysis of the amount of alkali consumed for the hydrolysis of the residual vinyl acetate. The viscosity of a 4 mass % aqueous solution was 41.5 mPa·s, and the average degree of polymerization was 2,400.

The obtained PVA dry powder was introduced into methanol in a bath ratio of 10, and separated by solid-liquid separation after being stirred for 3 hours. The resulting PVA powder (50% particle size of 500 μm, sodium acetate content of 0.05 parts) was vacuum dried at 90° C. until the volatile content was 1% or less.

The sodium acetate content was determined through neutralization titration of a solution of the PVA powder in water with hydrochloric acid, using methyl orange as an indicator.

The obtained PVA dry powder was then pulverized to the target size via collision using a BI mill (available from MicroPowtec), and PVA fine particles (pulverized product) were obtained.

The particle size of the obtained PVA fine particles was measured with a laser diffraction particle size distribution measurement device (LMS-3000 available from Malvern) under a dispersive pressure of 2 to 4 bar over a time period of 1 second. The 50% particle size (D50) was 96 μm.

NMR Measurement

The obtained PVA dry powder was charged into a zireonia rotor having a diameter of 4 mm after adding the same amount of n-decane. Measurements were made at room temperature at a rotor rotation speed of 5,000 Hz under the conditions shown in Table 2. The obtained spectrum was separated into waveforms using a Gaussian function at 46 ppm, 41 ppm, 36 ppm, and 21 ppm, and the area of each waveform was calculated. The gauche structure, and the degree of saponification were calculated according to the following formulae (2) and (3).

The waveforms of the peaks are shown in FIG. **2**.

$$\text{Gauche structure (mol \%)} = 100 \times (B/2+C)/(A+B+C) \quad (2)$$

(In formula (2), A represents the peak area at 46 ppm, B represents the peak area at 41 ppm, and C represents the peak area at 36 ppm.)

$$\text{Degree of saponification (mol \%)} = 100 \times (1-D/(A+B+C)) \quad (3)$$

(In formula (3), A represents the peak area at 46 ppm, B represents the peak area at 41 ppm, C represents the peak area at 36 ppm, and D represents the peak area at 21 ppm.)

TABLE 2

Measurement conditions	
Device Probe	Bruker AVANCEIII 400WB CP/MAS probe (ϕ = 4 mm)
Temperature	Room temperature (22° C.)
Medium	n-clecane
Observed nucleus	^{13}C
Rotation of sample tube	5,000 Hz
^{1}H 90° pulse	4.2 μs
Contact time	350 μs
τt	72 μs
τd	1 ms, 20 ms, 50 ms, 100 ms
FID signal capture time	14 ms
Runs	>3,000
Observation center	120 ppm
Observation range	365 ppm
Waiting time	20 s

Tablet Production

100 Parts of the obtained PVA fine particles, 100 parts of metformin hydrochloride, and 70 parts of crystalline cellulose (PH102 available from Asahi Kasei Chemicals Corporation) were mixed. The mixture was dissolved in IPA (isopropyl alcohol) and water (mass ratio of 50/50) with 30 parts of polyvinylpyrrolidone (PVP K 30 available from BASF) which is a solvent, using a granulator (Rapid Mixer Granulator available from Gem Pharma Machineries). After adding an appropriate amount, the mixture was granulated. The granules were dried with a Tray dryer (available from Bombay Machines) until the residual moisture was 2 to 4 w/w %, and a granulated material was obtained.

The granulated material was mixed with 30 parts of crystalline cellulose PH102, 3 parts of Aerosil, and 1 part of magnesium stearate, and an ellipsoidal tablet (measuring 1.9 cm in length, 0.9 cm in width, and 0.5 cm in height) was produced using a rotary tablet press.

The tablet was measured for hardness, friability, molded shape, and dissolution time. The results are shown in Table 3. The tablet was also evaluated for sustained release. The result is shown in FIG. **4**.

Comparative Example 1

A polyvinyl alcohol powder (degree of saponification: 87.7 mol %, the viscosity of a 4 mass % aqueous solution: 41.5 mPa·s) was pulverized, introduced into methanol in a bath ratio of 10, and stirred for 3 hours. After solid-liquid separation, the resulting PVA fine particles were vacuum dried at 90° C. until the volatile content was 1% or less. This produced PVA fine particles.

The 50% particle size (D50) was 100 μm as measured with a laser diffraction particle size distribution measurement device.

The gauche structure and the degree of saponification were determined by calculations through NMR measurements performed in the same manner as in Example 1. The waveforms are shown in FIG. **3**.

The PVA was used to produce a tablet, and the tablet was evaluated, as in Example 1. The results are shown in Table 3. The result of a sustained release test is shown in FIG. **4**.

Example 2

500 Parts of metformin hydrochloride was dissolved in IPA and water (mass ratio of 50/50) with 100 parts of polyvinylpyrrolidone (PVP K 30 available from BASF) which is a solvent, using a granulator (Rapid Mixer Granulator available from Gem Pharma Machineries). After adding an appropriate amount, the mixture was granulated.

The granulated material was mixed with 500 parts of the PVA fine particles obtained in Example 1, and 10 parts of magnesium stearate. An ellipsoidal tablet (measuring 1.9 cm in length, 0.9 cm in width, and 0.5 cm in height) was then produced using a rotary tablet press.

The tablet was evaluated in the same manner as in Example 1. The results are shown in Table 3. The result of a sustained release test is shown in FIG. **5**.

Comparative Example 2

The PVA fine particles produced in Comparative Example 1 were used to produce a tablet in the same manner as in Example 2, and the tablet was evaluated. The results are shown in Table 3. The result of a sustained release test is shown in FIG. **5**.

TABLE 3

	Particle size (μm)	Hardness (kg)	Friability (%)	Shape of molded tablet	Gauche structure (mol %)	Degree of surface saponification (rnol %)	Ratio of saponification degrees (average/surface)
Ex. 1	96	5	0.1	Smooth	36	78	1.14
Com. Ex. 1	100	3	0.2	Rough	23	82	1.08
Ex. 2	96	5	1.6	Smooth	36	78	1.14
Com. Ex. 2	100	1	4	Rough	23	82	1.08

By comparing Example 1 and Comparative Example 1 in which the PVA fine particles were added at the time of granulation, the tablet of Example 1 had more desirable hardness and friability than the tablet of Comparative Example 1, despite that the particle sizes were about the same.

The obtained tablet also had a smoother surface. The performance level of sustained release was about the same in Example 1 and Comparative Example 1.

By comparing Example 2 and Comparative Example 2 in which the PVA fine powder was added at the time of compression molding after granulation, the tablet of Example 2 had more desirable hardness and friability than the tablet of Comparative Example 2, despite that the particle sizes were about the same. The tablet of Example 2 also had a smoother surface. The performance level of sustained release was more desirable in Example 2 than in Comparative Example 2.

As demonstrated above, by using the medical binder as the PVA fine particles of the present invention, a tablet of desirable properties including moldability, hardness, sustained release, and friability can be obtained.

While the present invention has been described in detail and with reference to a certain embodiment of the invention, it will be apparent to a skilled person that various changes and modifications may be made thereto without departing from the spirit and scope of the invention. The present application is based on Japanese Patent Application No. 2014-152290 filed on Jul. 25, 2014, the entire contents of which are hereby incorporated by reference.

The invention claimed is:

1. A polyvinyl alcohol fine particle, comprising: 25 mol % or more of a gauche structure in polyvinyl alcohol molecules within a 0.8-nm region inside the particle from the particle surface wherein the ratio (S1/S2) of an average degree of saponification (S1) of the polyvinyl alcohol fine particle to an average degree of surface saponification (S2) in the 0.8-nm region inside the particle from the particle surface is 1.10 or more.

2. The polyvinyl alcohol fine particle according to claim **1**, which is obtained by pulverizing a dry powder of a polyvinyl alcohol consisting of solely a vinyl alcohol structure unit and a vinyl ester structure unit.

3. The polyvinyl alcohol fine particle according to claim **2**, wherein a 50% particle size of the dry powder of the polyvinyl alcohol is 50 to 2,000 μm.

4. The polyvinyl alcohol fine particle according to claim **1**, wherein a 50% particle size of the polyvinyl alcohol fine particle is 1 to 200 μm.

5. The polyvinyl alcohol fine particle according to claim **1**, which has an average degree of polymerization of 200 to 4,000.

6. The polyvinyl alcohol fine particle according to claim **1**, comprising: an alkali metal salt in an amount of 0.001 to 2 mass % of the polyvinyl alcohol fine particle.

7. A pharmaceutical binder, comprising: the polyvinyl alcohol fine particle of claim **1**.

8. A pharmaceutical tablet, comprising: an active ingredient; and the pharmaceutical binder of claim **7**.

9. A sustained-release pharmaceutical tablet, comprising: an active ingredient; and the pharmaceutical binder of claim **7**.

10. A method for producing the polyvinyl alcohol fine particle according to claim **1**, comprising: washing and drying a polyvinyl alcohol obtained from a vinyl alcohol structure unit and a vinyl ester structure unit, and pulverizing an obtained dry powder of the polyvinyl alcohol.

* * * * *

From:	Alsobrook, Lisa P.
To:	Gaynor, Paulette M
Cc:	Drozen, Melvin S.
Subject:	FW: GRN 927 - FDA items for clarification
Date:	Wednesday, September 2, 2020 9:42:23 AM
Attachments:	image001.png image002.png image003.png image004.png image005.png image006.png

Dear Dr. Gaynor,

We are writing on behalf of our client, Adept, to provide most of the clarifying information requested by the Food and Drug Administration (FDA) regarding the Generally Recognized as Safe (GRAS) notice, filed June 15, 2020 as GRN 927, for polyvinyl alcohol (PVOH) for use as a component of Adept's water-soluble, plugs for use in abattoirs to plug the anus of slaughtered sheep, lambs, and hogs for the purpose of blocking the exit of fecal material to prevent contamination of the carcass by intestinal contents during dressing. Specifically, we have responded in red text beneath items 2, 4, 5, 6, 7, and 8 in your August 19, 2020 email below. In this regard, as the clarifications provided below impact several sections of the GRAS notice, please let us know if it would be helpful for us to provide a PDF of the complete GRAS notice with revised parts to reflect all of the clarifications provided.

For items 1 and 3, Adept is waiting for its PVOH supplier to provide the additional information necessary to respond in full. The supplier has dedicated a technical team for processing Adept's request but has not provided a firm timeline. Therefore, and because Adept has encountered logistical issues, we respectfully request an extension of an additional 20 business days for responding in full to items 1 and 3 in your August 19, 2020 email below.

We hope and trust that the information provided below fully addresses FDA's questions 2, 4, 5, 6, 7, and 8, and that FDA is able to grant an extension of the due date while Adept's supplier works to gather the information necessary for responding to questions 1 and 3. And again, please let us know if FDA would like a clean copy of the GRAS notice with revised parts to reflect the clarifications provided in red text below.

Sincerely,

Lisa Alsobrook and Mel Drozen

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1001 G Street NW, Suite 500 West | Washington, DC 20001

From: Drozen, Melvin S. <Drozen@khlaw.com>
Sent: Wednesday, August 19, 2020 4:03 PM
To: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>

Cc: Alsobrook, Lisa P. <alsobrook@khlaw.com>
Subject: RE: GRN 927 - FDA items for clarification

From: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Sent: Wednesday, August 19, 2020 3:03 PM
To: Drozen, Melvin S. <Drozen@khlaw.com>
Subject: GRN 927 - FDA items for clarification

Dear Mr. Drozen,

As FDA continues with our evaluation of GRN 927, we have identified the following items that require clarification.

1. Adept Limited (Adept) states that "residual vinyl acetate in PVOH is not detected at the limit of detection (LOD) of the method of 1 ppm." In order to support the absence of unreacted vinyl acetate monomer in the PVOH polymer, please clarify what analytical method is used to analyze for vinyl acetate, as well as provide analytical results from five nonconsecutive representative batches to demonstrate that no residual vinyl acetate remains in the PVOH polymer.

   A complete response to this question requires information which is pending from Adept's supplier of the PVOH.

2. According to the certificate of analysis (COAs) in Appendix 1, Adept has conducted analyses for particle size of PVOH. However, Adept did not include particle size distribution in their proposed specifications for PVOH. We consider that particle size distribution of PVOH is important in understanding its physical and chemical properties. Further, in order to comply with specifications in the Food Chemical Codex (FCC 11th) and JECFA monographs (2007), we request Adept include the particle size distribution in the proposed specifications for PVOH.

   Adept agrees to include the FCC's specific test and criterion for particle distribution which were inadvertently omitted from the proposed specifications set forth in the March 27, 2020 GRAS notice. We will be happy to provide a revised Part 2.3 (Specifications for food-grade PVOH) if it would be helpful.

3. Please confirm that all analytical methods are validated for their intended use.

   A complete response to this question requires information which is pending from Adept's supplier of the PVOH.

4. We note that two different levels of PVOH (59% and 51%) in the plug formulation were used for the dietary exposure estimates. Additionally, Adept states in Part 4, Self-limiting levels of use that PVOH comprises 51% of the plug formulation. Please clarify the level for PVOH in the plug formulation and state the level of PVOH that is self-limiting for this use of PVOH.

   The level of PVOH in the plug formulation is 48% to 59%. Thus, the level of 59% is self-limiting for the intended use of PVOH. We will be happy to provide revisions for all parts of the GRAS notice that mention 51%, changing all of these to 59% and making any other changes to reflect this change.

5. In closing the part of the notice for the dietary exposure, Adept mentions an ADI, though does not state the source for that ADI. Later in the part of the notice for the narrative,

Adept discusses an ADI from JECFA. Please confirm whether the ADI that Adept mentions in the part of the notice for the dietary exposure is that from JECFA. However, if there was another source for this ADI, then please provide appropriate details.

Adept agrees with the acceptable daily intake (ADI) of 50 mg/kg bw/day that was determined by JECFA based on published feeding studies in rats. See GRN 927 at Part 6.3 (Basis for GRAS conclusion) on page 22. JECFA identified a No-Observed-Effect-Level (NOEL) of 5000 mg/kg bw/day for polyvinyl alcohol based on the maximum dose tested in both (1) the 90-day study in rats (i.e., Kelly et al. (2003), see GRN 927 Part 6.2.3 (Subchronic toxicity) at page 19) and (2) the two-generation study in rats (i.e., Rodwell et al. (2003), see GRN 927 Part 6.2.6 (Reproduction and Developmental Toxicity) at pages 20-21), and established an ADI for polyvinyl alcohol of 50 mg/kg bw/day, based on the NOEL of 5000 mg/kg bw/day from the subchronic toxicity and two-generation studies in rats, with a safety factor of 100. See GRN 927 Part 6.1.2 (JECFA review). There is no other source for the ADI of 50 mg/kg bw/day aside from the two published studies, which are discussed in the GRAS notice and which were the basis of the ADI determined by JECFA. We will be happy to provide a revised safety narrative (Part 6) to clarify the source for the ADI (Q5), give details on the updated literature search (Q6), and explain/elaborate on the conclusion regarding no carcinogenicity concerns (Q8).

6. While Adept's notice refers to a literature search for a previous notice (i.e., GRN 767), it does not appear to contain information about Adept's literature searches. Please describe literature searches conducted by Adept which were the bases for the safety analysis in sections 6.2, 6.3 and 6.4. Within this description, please describe the databases searched, the search terms used, and the time period covered.

An extensive search of the world literature was initially conducted on February 5, 2019 in preparing this GRAS notice, and repeated on August 20, 2020 after submission of the GRAS notice, and included the search terms as follows:

- Key search terms: polyvinyl alcohol, vinyl alcohol polymer, PVOH, 9002-89-5, methanol, methyl acetate, toxicokinetics, toxicity,
- Refining search terms (depending on output of key term search): absorption, distribution, metabolism, oral, ingestion, acute, subacute, subchronic, chronic, carcinogenicity, tumor promotion, genotoxicity, mutagenicity, clastogenicity, reproductive, developmental, irritation, hypersensitivity, allergy, neurotoxicity

The key search engines used included:

- PubMed (http://www.ncbi.nlm.nih.gov/pubmed)
- Toxnet (https://www.nlm.nih.gov/toxnet/index.html; includes HSDB, Toxline, ChemID Plus, and DART in Toxnet)
- ECHA (European Chemicals Agency – REACH dossiers) (https://echa.europa.eu/information-on-chemicals/registered-substances)

Other data sources searched for the key terms poly vinyl alcohol and/or 900-89-5 were:

- Cosmetic Ingredient Review (CIR) (https://www.cir-safety.org/ingredients)
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) (http://www.ecetoc.org/)

- eCFR (https://www.ecfr.gov/cgi-bin/ECFR?page=browse)
- EFSA Opinions (http://www.efsa.europa.eu/en/publications)
- FAO (Food and Agriculture Organization of the United Nations) (http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/)
- Google Scholar (https://scholar.google.com/)
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- International Programme on Chemical Safety (http://www.inchem.org/#)
- IUCLID (International Uniform Chemical Information Database) - https://iuclid6.echa.europa.eu/search
- NICNAS (Australian National Industrial Chemical Notification and Assessment Scheme) (https://www.industrialchemicals.gov.au/)
- NIOSH (National Institute for Occupational Safety and Health) (https://www.cdc.gov/niosh/topics/chemical.html)
- NTIS (National Technical Information Service) (http://www.ntis.gov/)
- NTP (National Toxicology Program) (https://ntp.niehs.nih.gov/)
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets) (https://hpvchemicals.oecd.org/ui/Search.aspx)
- SCCS (Scientific Committee for Consumer Safety) opinions: (http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm)
- SCOGS DB (https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=SCOGS
- Substances Added to Foods (https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=FoodSubstances)

7. A publication (i.e., "Sanders and Matthews (2009)) cited in the discussion of ADME (section 6.2.1, page 18) is not included in the reference list (section 7.1). Please provide a full citation of this reference or give appropriate clarification.

The full citation is as follows: Sanders, J.M., Matthews, H.B. 1990. Vaginal absorption of polyvinyl alcohol in Fischer 344 rats. Hum Exp Toxicol 9: 71-77. We will be happy to provide a revised list of references, to include the citation for Sanders (1990), if it would be helpful.

8. On page 20, Adept concludes that the absence of carcinogenic activity reported in an NTP bioassay with intra-vaginal exposure to polyvinyl alcohol "indicates that polyvinyl alcohol is not carcinogenic [and] does not pose a carcinogenic risk from dietary exposures to this ingredient." Please provide a brief narrative to explain the basis of Adept's extrapolation from one route of exposure (intra-vaginal) to another (oral) with toxicokinetic information, such as the low oral absorption elaborated in Section 6.2.1.

In the published literature, no chronic toxicity or carcinogenicity studies were found following oral administration of polyvinyl alcohol. In a well-designed 2-year National Toxicology Program study (NTP; 1998) no treatment related neoplasms or nonneoplastic lesions were found in the reproductive system or other internal or external organs of female B6C3F1 mice receiving 20 µl 25% aqueous PVOH/day 5 days/week intravaginally for 2 years. The only clinical finding observed in this study was vaginal irritation. NTP concluded that there was no evidence that the low-viscosity PVOH (molecular weight approximately 24,000) has carcinogenic activity in this study.

As noted by NTP (1998), PVOH is used in surgical drapes, towels, and gauze sponges; protective gloves; cosmetic formulations; topical ophthalmic preparations; plastic sponge implants for

reconstructive surgery, and intravaginal contraceptive foam and film. Furthermore, PVOH is used with magnesium sulfate to dilate the cervix of women prior to induction of labor. Hundreds of thousands of women in the United States use an intravaginal product containing PVOH each year. The FDA nominated low-viscosity polyvinyl alcohol for a 2-year study because of concern about the lack of information about the long-term toxic and carcinogenic effects by the intravaginal route.

The results of the NTP (1998) study are consistent with the observations from oral exposure studies demonstrating that PVOH is not absorbed systemically through the mucosa of the gastrointestinal tract and with the absence of genotoxicity observed in the genotoxicity tests of PVOH. Specifically, negligible absorption of PVOH through the vaginal mucosal surface, which is inferred from the demonstrated absence of absorption of PVOH through the mucosa of the gastrointestinal tract in oral studies, helps to explain the absence of any exposure-related lesions of the internal organs of the treated animals in the NTP study. Furthermore, the absence of neoplastic lesions in the internal and external organs of the intra-vaginally exposed mice, including on the directly exposed vaginal mucosal surface, is consistent with the lack of genotoxicity demonstrated in genotoxicity tests.

Based on the low absorption rate of polyvinyl alcohol through the mucosa of the gastrointestinal tract (discussed in Part 6.2.1.), the absence of genotoxicity concerns (discussed in Part 6.2.4.), and the results of the NTP study showing no neoplastic lesions in the internal and external organs of the intra-vaginally exposed mice, including on the *directly exposed* vaginal mucosal surface, Adept concludes there is no evidence that polyvinyl alcohol is carcinogenic and that polyvinyl does not pose a carcinogenic risk from dietary exposures.

If it would be helpful, we will be happy to provide a new safety narrative to replace the existing Part 6.2.5 with the more clear discussion above.

If you or Adept have any questions about the items that require clarification, please let me know. FDA respectfully requests a response within 10 business days. If unable to complete the response within that timeframe, please contact me. Thank you.

Sincerely,
Paulette Gaynor

Paulette M. Gaynor, Ph.D.
Senior Policy Advisor

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety, Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-1192
Paulette.Gaynor@fda.hhs.gov

From:	Drozen, Melvin S.
To:	Gaynor, Paulette M
Cc:	Alsobrook, Lisa P.
Subject:	GRN 927/FSIS Questions
Date:	Tuesday, September 15, 2020 3:04:08 PM
Attachments:	JECFA 2004.pdf Ollari & Conti, Fatend Flushing System.pdf Topic6+Casings+28May.pdf

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Dear Dr. Gaynor,

The purpose of this email is to provide additional information regarding the two remaining points of concern to FSIS, as outlined in your September 1, 2020 email below. Specifically, underneath your recap of FSIS's original questions (one regarding residual PVOH and another regarding possible technical functions), the NOTIFIER's RESPONSE to each question, and the FSIS response, we have added additional information under the heading "Notifier's Additional Response" for each of the two questions. We trust that this additional information provides adequate support, in the form of compelling evidence that it is not realistic to expect polyvinyl alcohol (PVOH) to become a component of food under the intended conditions of use. The responses, if you scroll down below, also speak to the impossibility of any technical effect in food because film formation or binding is not feasible in this application, and also because no PVOH would be present in food to perform any such functions. Additionally, as noted in the responses below, we have attached PDFs for information that is referenced to reinforce critical points for understanding that PVOH is not reasonably expected to become a component of food under the intended conditions of use.

Best regards,

Mel Drozen and Lisa Alsobrook.

From: Drozen, Melvin S. <Drozen@khlaw.com>
Sent: Tuesday, September 1, 2020 5:47 PM
To: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Cc: Alsobrook, Lisa P. <alsobrook@khlaw.com>
Subject: RE: additional from FSIS - GRN 927

Dear Dr. Gaynor,

Thank you for your email. We will get back to you as soon as possible. Regards. Mel Drozen.

Melvin S. Drozen
Partner
tel: +1 202.434.4222 | fax: +1 202.434.4646 | drozen@khlaw.com
1001 G Street NW, Suite 500 West | Washington, DC 20001

From: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Sent: Tuesday, September 1, 2020 5:14 PM
To: Drozen, Melvin S. <Drozen@khlaw.com>
Subject: additional from FSIS - GRN 927

Dear Mr. Drozen,

FSIS has informed FDA that additional information is still needed concerning some of their questions. Please see below for these two points from FSIS.

FSIS originally asked----1% is used as a worst case scenario for residual product left on the intestines. How was that number estimated, i.e., does the notifier have any studies showing what the actual amount of PVOH that remains after washing?

Notifier's RESPONSE: No amount of PVOH is expected to remain after washing. As noted at page 10 of the GRAS notice, due to the high molecular weight of material (22,000 to 27,000 g/mol), any dissolved PVOH from the plug making direct contact with the inner surface of the bung during slaughter will not penetrate the surface of the intestinal tissue to any significant extent and will be amenable to complete removal through the washing step. Any washing process that is sufficient to remove fecal material (as required for the meat to be considered clean) would also reasonably be expected to remove components of the water-soluble plug. As no data are available to demonstrate that the level of residue is absolutely 0.00% or lower, however, the level of 1% was chosen as a worst-case exaggeration, solely for the purpose of establishing the safety of any unexpected *de minimis* traces of plug material. Based on the weight of a plug (5 grams), this amount (1%) is 50 milligrams (the same weight as about 25 mosquitoes). In this regard, we may assume that such residue would be an intact piece and would be easily visible since the dissolved portion of the plug would be even more likely to be washed away with the fecal material. Accordingly, although the number, 1%, is not based on studies, it surely represents a great exaggeration of the level of PVOH, if any, that may actually remain after washing.

FSIS response. As there is no data on the amount of residue, all the assumptions made here are unsupported. Therefore, it cannot be concluded that 1% is a reasonable estimate of the level of PVOH that may remain after washing . The amount of residue that would be left behind is completely unknown. Please provide data supporting the amount of PVOH residue left that may

remain after washing.

Notifier's Additional Response:

Adept realizes that the level of "1%" is purely an assumption, but it is reasonable to adopt such an exaggerative estimate of the possible amount of polyvinyl alcohol (PVOH) residue that could possibly be present on food that is in very brief contact with the PVOH plug because of the value in having some "worst-case" number for comparison with the acceptable daily intake (ADI) of PVOH in reaching a safety conclusion. By assuming a residual level of PVOH of 1% for purposes of a safety assessment, however, we did not mean to imply that any PVOH would in fact remain on casings or hog bung from animals processed using the water-soluble plug. On the contrary, based on the enormous volume of water in comparison to the volume of the plug, as discussed in greater detail below, it is not at all reasonable to expect that any measurable amount of PVOH could remain after the material at issue is squeezed, cleaned, and flushed out as required to remove fecal matter. Further, the (mucosal) layer of the large intestine, which is in direct contact with the PVOH plug during use, is removed in preparing casings. Thus, any PVOH assumed to remain on the mucosal surface after using the plug and thorough rinsing of the mucosal surface immediately thereafter will be discarded with the sloughed off mucosal lining during the manufacturing of the casing.

We recognize that in such a case, where no detectable residue is reasonably expected, it would alternatively be acceptable to adopt the limit of detection (LOD) for an analytical method as the "worst-case" number for assessing the safety of potential dietary exposure. However, no standardized test methods are available for the determination of PVOH. See JECFA report (2004) available at http://www.fao.org/fileadmin/templates/agns/pdf/jecfa/cta/61/PVA.pdf (PDF attached). While semi-quantitative methods are available for detecting PVOH in wastewater from textile and paper mills (International Journal of Environ. Analytical Chemistry, 2013) and in pharmaceutical solutions (Current Pharmaceutical Analysis, 2020), our chemists have advised that these methods could not be readily adapted to provide reliable estimates of low concentrations of PVOH in a food matrix.

Even if it were possible to overcome the technological challenges of a quantitative analysis for PVOH, it is technologically impossible to conclude that absolutely "zero" PVOH residue remains on the finished food in this case. In any event, the expectation that any potential plug residues will be washed away is fully supported by consideration of the processing methods for the casings and hog bung. As described in further detail below, the cleaning process for bung portions and intestines used for casings is so water intensive that there is no reasonable expectation of finding detectable PVOH residue.

It is also worth noting that PVOH, as a component of Adept's water-soluble plugs, is not being used to effect any change in the food, and even to the extent that some small amount of residue could dissolve at the plug-and-intestine surface interface, no technical function is expected before such residue would be completely washed away. In this regard, in the 2004 report noted above, JECFA reviewed PVOH with a degree of hydrolysis (86.5 – 89%), which is the same as the grade at issue here, and a molecular weight range (26,300 – 30,000) that is comparable, i.e., 22,000 – 27,000 g/mol, for use at a level of 2.3 mg /cm^2 as a component of a moisture barrier film for food

supplement tablets and for foods that contain inclusions or dry food with inclusions that need to be protected from moisture uptake. Although it is not stated in the report, when such moisture barrier films dissolve, they do not reform and the PVOH has no ongoing technical effect. Thus, based on compositional similarities to the PVOH described in the JECFA report, the grade of PVOH used in Adept's plugs would likely be suitable for use as a component of a moisture barrier film. The PVOH could, however, be useful only as one component of such a multi-ingredient film and there is no expectation that PVOH residue from a dissolved plug, without employing any film conversion equipment or mixing it in a controlled manner with other ingredients, would on its own form into a moisture barrier film or have any particular affinity for meat tissue. To our knowledge, there is no grade of PVOH that has ever been investigated as a processing aid or food additive for any conceivable technical function in casings or hog bungs. The full expectation is that PVOH has no technical function in the proposed application aside from serving as the constituent of an intact water-soluble plug intended for brief contact with the lumenal surface of the rectum and bung portion of slaughtered hogs and sheep to prevent contamination of the meat with fecal matter during the slaughter of food-producing animals.

The water-soluble plugs initially function in the same manner as other, non-water-soluble plugs that may currently be used, i.e., they achieve a tight fit that blocks fecal matter. Specifically, the plugs are designed to remain intact, thereby blocking feces, for the short time they are in contact with the entire circumference of the rectum and terminal straight end section of the large intestine (*i.e.*, "bung portions") of sheep, lambs, and hogs after post-slaughter insertion of the plugs into the rectum. For example, in the case of a plant slaughtering 500 hogs per hour (which is slower than the current limit of 1,106 hogs per hour), the plug would be in place for merely 7.2 seconds. By comparison, the plug does not begin to dissolve until after 5 minutes in 100 mL of water under stirring (with a magnetic stirrer at 100 rpm) at 37°C (98.6^{O}F). Thus, under the usual expected operating parameters, a water-soluble plug would remain intact until after it is physically removed, along with feces and other waste, such as fatty tissue and mucosal tissue. After removal, the plug dissolves over time in wastewater. Further, to the extent that any portion of the plug could begin to partially soften or dissolve while inside the slaughtered animal, we note that the manufacturing process uses a very large quantity of water for purposefully removing residue (fecal matter) from the material at issue. Such processing would incidentally remove all PVOH residue, if any, at the same time because PVOH does not have any particular binding affinity for animal tissue, as noted above, and is fully water soluble. Additionally, fully cleaned casings are packed in a saturated salt solution for storage prior to further processing. The casings are flushed to remove the salt before use in stuffing sausages, which is an additional process that would also remove other substances, such as PVOH residue, if any. The sheer volume of water in comparison to the volume of the plug, however, counsels that it is highly unlikely that any PVOH residue would remain on cleaned tissue even before a rinsing step that is necessary to remove salt.

The plugs are 12cm (length) with a diameter of 4 cm (at the flanges). Thus, the volume of the bung section that contacts the plug is 150.8 cm^3, or roughly 150 mL. By comparison, for example, the technical specification on water consumption for an automatic hog bung (fat-end) flushing system that can process 1,250 hogs per hour (20 to 21 hogs per minute) is 100 liters/minute. See http://www.ollarieconti.it/index.php?option=com_content&view=article&id=222&Itemid=474&lang=en (PDF attached). Thus, at least 4.7

liters of water per hog would be used by this equipment to flush the hog bung; an amount that is more than 31 times larger than the volume of the area that is in contact with the plug. Because no fecal matter is permitted on casings or bung meat, other processing equipment besides the example given would be expected to use a similar volume of water. Moreover, in addition to cleaning/washing/flushing processes, for those portions of hog or sheep intestines that are used as casings, the inner layer and outer layers are removed such that only the collagen layer, i.e., the sub-mucosa, remains. (Steps for conversion of hog and sheep intestines to natural casings is described in a May 2010 publication by the Scottish government, available at https://www.qmscotland.co.uk/sites/default/files/Topic6+Casings+28May.pdf, PDF attached). Thus, since only a relatively short section of the inner layer (i.e., mucosa) would contact a water-soluble plug, any PVOH residue that could possibly dissolve in the short interval between insertion of the plug and processing would be removed with the mucosal layer.

We ask FSIS to recognize that the additional information provided above on the volume of the plug in comparison to the volume of water used for cleaning, as well as other processes that are necessary to convert the food-contact surfaces (i.e., rectum and bung portions) to edible food, supports the reasonable conclusion that no detectable residue of PVOH can reasonably be expected to be present in the finished food.

FSIS originally asked----Polyvinyl alcohol is used in some applications as a binder, for example in consumable tablets. Is there data or scientific literature available to support that PVOH would have no technical effect as a binder at 0.0059%, the estimated highest level remaining in the finished product?

Notifier's RESPONSE: Polyvinyl alcohol may be used as a *temporary* binder in tablets. Such tablets must be protected from moisture to keep the tablet from dissolving. Thus, PVOH at any level would not be an effective binder in the meat at issue. Further, the level of PVOH necessary for functioning as a binder in consumable tablets appears to be well above 0.0059%. For example, Patent WO2016013675A1 shows tablet formulation using 100 parts of PVOH to 270 parts (combined) of other ingredients, or around 33% PVOH in the tablet. Lower levels of PVOH may have a technical function in other products besides tablets. For example, a product brochure from Millipore indicates that PVOH was studied for use as a thickener in ophthalmic solutions using test samples containing 4%, 10%, and higher concentrations of polyvinyl alcohol. We found no examples of PVOH being used for any technical function at levels lower than 3% (a level at which the Millipore brochure indicates that certain grades of PVOH may help with solubility of the active pharmaceutical ingredient in liquid forms).

FSIS response--As per the Sekisui brochure "Polyvinyl Alcohol in Emulsion Polymerization", and information found on Millipore's website, PVOH has a range of technical effects which are dependent on the molecular weight and degree of hydrolysis, many of which would be considered technical effects which require labeling in meat and poultry products, including stabilization of emulsions, texturizing, and gelling. Gelling agents commonly act as binders. Information on common levels of use is not supportive of a minimum level at which a technical effect may present. FSIS does not recognize a minimum level below which ingredients are considered to have no technical effect, as this is highly variable and some substances have been shown to provide technical effects at very

low levels.

Please provide data to support what amount, if any, residue is present at the conclusion of the washing process. If no residue is detectable, no further information is needed. If there is detectable residue, scientific information should be provided to support that the amount present in total formulation meets the definition of a processing aid as per 21 CFR 101.100(a)(3).

As discussed in the Compliance Guide on the Determination of Processing Aids, "Processing aids are defined as: (a) substances that are added during the processing of a food but are removed in some manner from the food before it is packaged in its finished form; (b) substances that are added to a food during processing, are converted into constituents normally present in the food, and do not significantly increase the amount of the constituents naturally found in the food; or (c) substances that are added to a food for their technical or functional effect in the processing but are present in the finished food at insignificant levels and do not have any technical or functional effect in that food."

PVOH is not a constituent normally found in food, and if residue is detectable it would indicate the substance is not removed from the food before it is packaged in its finished form. Therefore, submitter would likely need to support that it is a substance that is "added to a food for their technical or functional effect in the processing but are present in the finished food at insignificant levels and do not have any technical or functional effect in that food." Submitter would need to provide a scientifically supported explanation of why the variety of PVOH in use in the plugs does not provide a technical effect that would require labeling or, if this variety of PVOH does have the potential produce a technical effect, data to support that their PVOH product would not provide a technical effect at those levels. Otherwise, the PVOH would require labeling.

Notifier's Additional Response: As discussed above, Adept has determined based on scientific reasoning that PVOH is not reasonably expected to remain at detectable levels in the finished food.

Please send the response to me, and I will convey to FSIS.

Sincerely,
Paulette Gaynor

Paulette M. Gaynor, Ph.D.
Senior Policy Advisor

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety, Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-1192
Paulette.Gaynor@fda.hhs.gov

Three pages have been removed in accordance with copyright laws. The removed reference citations is:

Joint FAO/WHO Expert Committee on Food Additives (JECFA), Polyvinyl Alcohol (PVA), Chemical and Technical Assessment, 61st JECFA (2004) available at http://www.fao.org/fileadmin/templates/agns/pdf/jecfa/cta/61/PVA.pdf.

Automatic hog bung (fatend) flushing system MOD.VGA1250








The machine is suitable for the individual manual de-fatting by the worker, separation of the organs attached, automatic manure flushing and automatic cutting of the crown along with easy disposal of the waste product.

The Unit is composed of:

- A support structure in stainless steel
- S/s vertebrae chain supported by the frame. The speed of the chain is adjustable by an inverter to match the production capacity of the plant
- Special Injector Nozzles to support of the rectum mounted on the vertebrae chain with stainless steel guides to support the rectum throughout the rotation, while at the first curve automatically allowing the injection of water to flush the rectum
- Mechanical/Automatic water injection system for the flushing
- Motorized circular blade to cut the rectums crown
- Motorized brush to remove the crown from the nozzles
- Automatic Self-Cleaning system for the chain
- Security Barriers along the unit
- The machine can be equipped with belts, chutes, pumps, pneumatic conveyors (link) for the transport of the product and waste
- The unit is shipped in section for easy installation
- The operator must manually insert the rectum on the injector. The then hangs for the workers to manual trim the fat and organs where the flushing and cutting of the crown is done automatically
- Unless otherwise requested, comes complete with electrical panel wired with stainless steel cabinet, requiring only installing the final connections to the main power

Technical Characteristics:

- 400v, 3phase, 50hz, 2.1Kw
- Water Consumption: 100 liters/min.
- Up to 1250 heads per hour

From:	Drozen, Melvin S.
To:	Gaynor, Paulette M
Cc:	Alsobrook, Lisa P.
Subject:	GRN 927 - FDA items for clarification
Date:	Thursday, September 24, 2020 2:18:26 PM
Attachments:	image001.png image002.png image003.png image004.png image005.png image006.png Umeda 2004.pdf GRN 927, Part 2.3, revised 9-9-2020.pdf PVA_VAM_method__Full.pdf PVA BP05 Chromatographs.pdf

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Dear Dr. Gaynor,

This message and its attachments, along with our September 2, 2020 email below provide complete responses to the request for clarification by the Food and Drug Administration (FDA) regarding the Generally Recognized as Safe (GRAS) notice, filed June 15, 2020 as GRN 927, for polyvinyl alcohol (PVOH) for use as a component of our client's, Adept's, water-soluble, plugs for use in abattoirs to plug the anus of slaughtered sheep, lambs, and hogs for the purpose of blocking the exit of fecal material to prevent contamination of the carcass by intestinal contents during dressing. Our September 2, 2020 email provides responses in red text beneath items 2, 4, 5, 6, 7, and 8 in your August 19, 2020 email below. Regarding our response to item 2, at FDA's request we subsequently also provided the attached GRN 927, Part 2.3, revised 9-9-2020, which includes the complete particle size. For items 1 and 3, FDA granted more time for Adept to obtain information from its PVOH supplier. Items 1 and 3 are set forth in italics below with our responses beneath each item as follows:

1. *Adept Limited (Adept) states that "residual vinyl acetate in PVOH is not detected at the limit of detection (LOD) of the method of 1 ppm." In order to support the absence of unreacted vinyl acetate monomer in the PVOH polymer, please clarify what analytical method is used to analyze for vinyl acetate, as well as provide analytical results from five nonconsecutive representative batches to demonstrate that no residual vinyl acetate remains in the PVOH polymer.*

The saponification step that converts polyvinyl acetate to polyvinyl alcohol (PVOH) is efficient at destroying residual vinyl acetate monomer (VAM) and subsequent processing of the finished polymer further reduces trace residues. Adept's supplier does not routinely test for residual vinyl acetate monomer. Complete data on residual VAM were developed solely for the purpose of addressing FDA's request for clarification. The supplier had initially provided details to support the statement in GRN 927 on the non-detection of VAM in what appears to have been a perfunctory fashion and there were also translation issues that resulted in our including in error the statement "residual vinyl acetate in PVOH is not detected at the limit of detection (LOD) of the method of 1 ppm." In addition to providing the attached "PVA_VAM_method_Full" and "PVA BP05 Chromatograph," which provides the analytical method and results from five nonconsecutive representative batches, as FDA requested, we must correct the information previously provided regarding residual VAM.

-

Correction: Residual VAM is not expected to be present at detectable levels in the PVOH. This was confirmed by analytical data demonstrating that VAM was not detected in five nonconsecutive

representative batches of PVOH at a limit of detection (LOD) for the test method of 200 parts per million (ppm). The attached analytical method and analytical results are designated as **CONFIDENTIAL** by Adept's supplier and are provided by us to FDA on a **CONFIDENTIAL** basis. These **CONFIDENTIAL** data are supportive of Adept's GRAS conclusion but are not pivotal as the data merely illustrate there are no unexpected irregularities in the grade of PVOH used by Adept with respect to VAM as compared to other grades of PVOH on the market.

The test methods and specifications developed for the reference grade in the Food Chemicals Codex (FCC) monograph for polyvinyl alcohol are considered appropriate for the PVOH purchased by Adept for use in the plugs at issue. In this regard, VAM is not among the impurities for which testing and acceptance criteria are specified in the FCC monograph. Moreover, PVOH and any potential impurities that may be present are not expected to become a component of food under the intended conditions of use for Adept's plug. Nevertheless, if we assume that the total daily intake of PVOH from all food applications, including Adept's plugs, is 46.13 mg/kg bw/day (posited as a very conservative worst case in GRN 927), and that all of the PVOH contains VAM at a level of 200 ppm (i.e. 0.02%), the estimated daily intake (EDI) of VAM would be 9.2 µg/kg bw/day (i.e. 43.13 mg/kg bw/day x 0.02% ÷ 1000 µg/mg).

The International Agency for Research on Cancer (IARC, 1995) determined that there is inadequate evidence from epidemiological studies for the carcinogenicity of VAM and limited evidence from inhalation studies indicating increased nasal cavity tumors in rats. IARC (1995) classified VAM as possibly carcinogenic to humans (i.e. a Group 2 carcinogen) (http://www.inchem.org/documents/iarc/vol63/vinyl-acetate.html). Similarly, VAM has been judged to be a possible human carcinogen by the Japan Society for Occupational Health (JSOH) and a confirmed animal carcinogen with unknown relevance to humans by the American Conference of Governmental Industrial Hygienists (ACGIH).

Umeda et al. (2004) (attached) performed a combined chronic toxicity/carcinogenicity study in accordance with OECD TG453 and GLP in which rats and mice (n=50/sex/species/dose) were exposed to 0, 400, 2000, or 10,000 ppm VAM in the drinking water for 2 years. These concentrations corresponded, respectively, to 0, 42-63, 202-301, and 989-1418 mg/kg bw/day in the mice and 0, 21-31, 98-146, and 442-575 mg/kg bw/day in the rats. Tumors developed in the stratified squamous epithelium of the upper digestive tract of the males and females of both species in this study. Umeda et al. (2004) plotted the dose-response curve for the combined incidence of squamous cell carcinomas and papillomas in the oral cavity of males and females of both species. The dose-response curve revealed a discernable increase in tumor incidences in the animals exposed to >400 mg/kg bw/day VAM. These authors applied US EPA's Benchmark Dose Software v. 1.3.1 to calculate a $BMDL_{10}$ of 477 mg/kg bw/day for VAM based on a multistage model, which provided the best goodness-of-fit p-value among the model options.

The margin of exposure (MOE) for an EDI of 9.2 µg/kg bw/day based on the $BMDL_{10}$ of 477 mg/kg bw/day is 51,848 (477 mg/kg bw/day ÷ [9.2 µg/kg bw/day x 0.001 mg/µg]). Thus, any risks that may be associated with potential exposures to VAM in PVOH in foods, food supplements, and medicines would be negligible assuming a worst-case exposure scenario. Furthermore, the contribution of VAM from the use of the PVOH plug, if any (since no exposure is expected) would contribute a very small fraction to the overall dietary exposure to VAM from all PVOH sources.

3. *Please confirm that all analytical methods are validated for their intended use.*

The analytical method for VAM was validated as described in the attached **CONFIDENTIAL** "PVA_VAM_method_Full." No "re-validation" was performed for testing of the PVOH for compliance with the specifications adopted from the FCC monograph for PVOH. Instead, as indicated on the Certificates of Analysis provided in GRN 927, the testing lab followed the test methods described for each parameter in the FCC. Prior to the adoption of the noted procedures by the FCC as standardized methods for evaluating compliance with its specifications, validity for the stated purpose must be established. Accordingly, because the methods used are internationally recognized standard methods, we respectfully submit that additional validations confirming the appropriateness of the methods are unnecessary and would be redundant.

We hope and trust that the information provided in this email and its attachments fully addresses FDA's questions 1 and 3, and that the complete information provided to FDA will allow both FDA and USDA to favorably complete their reviews.

Please let us know if you have any further questions.

Sincerely,

Mel Drozen and Lisa Alsobrook.

From: Alsobrook, Lisa P.
Sent: Wednesday, September 2, 2020 9:42 AM
To: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Cc: Drozen, Melvin S. <Drozen@khlaw.com>
Subject: FW: GRN 927 - FDA items for clarification

Dear Dr. Gaynor,

We are writing on behalf of our client, Adept, to provide most of the clarifying information requested by the Food and Drug Administration (FDA) regarding the Generally Recognized as Safe (GRAS) notice, filed June 15, 2020 as GRN 927, for polyvinyl alcohol (PVOH) for use as a component of Adept's water-soluble, plugs for use in abattoirs to plug the anus of slaughtered sheep, lambs, and hogs for the purpose of blocking the exit of fecal material to prevent contamination of the carcass by intestinal contents during dressing. Specifically, we have responded in red text beneath items 2, 4, 5, 6, 7, and 8 in your August 19, 2020 email below. In this regard, as the clarifications provided below impact several sections of the GRAS notice, please let us know if it would be helpful for us to provide a PDF of the complete GRAS notice with revised parts to reflect all of the clarifications provided.

For items 1 and 3, Adept is waiting for its PVOH supplier to provide the additional information necessary to respond in full. The supplier has dedicated a technical team for processing Adept's request but has not provided a firm timeline. Therefore, and because Adept has encountered logistical

issues, we respectfully request an extension of an additional 20 business days for responding in full to items 1 and 3 in your August 19, 2020 email below.

We hope and trust that the information provided below fully addresses FDA's questions 2, 4, 5, 6, 7, and 8, and that FDA is able to grant an extension of the due date while Adept's supplier works to gather the information necessary for responding to questions 1 and 3. And again, please let us know if FDA would like a clean copy of the GRAS notice with revised parts to reflect the clarifications provided in red text below.

Sincerely,

Lisa Alsobrook and Mel Drozen

Lisa P. Alsobrook
Associate
Keller and Heckman LLP
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From: Drozen, Melvin S. <Drozen@khlaw.com>
Sent: Wednesday, August 19, 2020 4:03 PM
To: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Cc: Alsobrook, Lisa P. <alsobrook@khlaw.com>
Subject: RE: GRN 927 - FDA items for clarification

From: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Sent: Wednesday, August 19, 2020 3:03 PM
To: Drozen, Melvin S. <Drozen@khlaw.com>
Subject: GRN 927 - FDA items for clarification

Dear Mr. Drozen,

As FDA continues with our evaluation of GRN 927, we have identified the following items that require clarification.

1. Adept Limited (Adept) states that "residual vinyl acetate in PVOH is not detected at the limit of detection (LOD) of the method of 1 ppm." In order to support the absence of unreacted vinyl acetate monomer in the PVOH polymer, please clarify what analytical method is used to analyze for vinyl acetate, as well as provide analytical results from five nonconsecutive representative batches to demonstrate that no residual vinyl acetate remains in the PVOH polymer.

   A complete response to this question requires information which is pending from Adept's supplier of the PVOH.

2. According to the certificate of analysis (COAs) in Appendix 1, Adept has conducted analyses for particle size of PVOH. However, Adept did not include particle size distribution in their proposed specifications for PVOH. We consider that particle size distribution of PVOH is important in understanding its physical and chemical properties. Further, in order to comply

with specifications in the Food Chemical Codex (FCC 11th) and JECFA monographs (2007), we request Adept include the particle size distribution in the proposed specifications for PVOH.

Adept agrees to include the FCC's specific test and criterion for particle distribution which were inadvertently omitted from the proposed specifications set forth in the March 27, 2020 GRAS notice. We will be happy to provide a revised Part 2.3 (Specifications for food-grade PVOH) if it would be helpful.

3. Please confirm that all analytical methods are validated for their intended use.

A complete response to this question requires information which is pending from Adept's supplier of the PVOH.

4. We note that two different levels of PVOH (59% and 51%) in the plug formulation were used for the dietary exposure estimates. Additionally, Adept states in Part 4, Self-limiting levels of use that PVOH comprises 51% of the plug formulation. Please clarify the level for PVOH in the plug formulation and state the level of PVOH that is self-limiting for this use of PVOH.

The level of PVOH in the plug formulation is 48% to 59%. Thus, the level of 59% is self-limiting for the intended use of PVOH. We will be happy to provide revisions for all parts of the GRAS notice that mention 51%, changing all of these to 59% and making any other changes to reflect this change.

5. In closing the part of the notice for the dietary exposure, Adept mentions an ADI, though does not state the source for that ADI. Later in the part of the notice for the narrative, Adept discusses an ADI from JECFA. Please confirm whether the ADI that Adept mentions in the part of the notice for the dietary exposure is that from JECFA. However, if there was another source for this ADI, then please provide appropriate details.

Adept agrees with the acceptable daily intake (ADI) of 50 mg/kg bw/day that was determined by JECFA based on published feeding studies in rats. See GRN 927 at Part 6.3 (Basis for GRAS conclusion) on page 22. JECFA identified a No-Observed-Effect-Level (NOEL) of 5000 mg/kg bw/day for polyvinyl alcohol based on the maximum dose tested in both (1) the 90-day study in rats (i.e., Kelly et al. (2003), see GRN 927 Part 6.2.3 (Subchronic toxicity) at page 19) and (2) the two-generation study in rats (i.e., Rodwell et al. (2003), see GRN 927 Part 6.2.6 (Reproduction and Developmental Toxicity) at pages 20-21), and established an ADI for polyvinyl alcohol of 50 mg/kg bw/day, based on the NOEL of 5000 mg/kg bw/day from the subchronic toxicity and two-generation studies in rats, with a safety factor of 100. See GRN 927 Part 6.1.2 (JECFA review). There is no other source for the ADI of 50 mg/kg bw/day aside from the two published studies, which are discussed in the GRAS notice and which were the basis of the ADI determined by JECFA. We will be happy to provide a revised safety narrative (Part 6) to clarify the source for the ADI (Q5), give details on the updated literature search (Q6), and explain/elaborate on the conclusion regarding no carcinogenicity concerns (Q8).

6. While Adept's notice refers to a literature search for a previous notice (i.e., GRN 767), it does not appear to contain information about Adept's literature searches. Please describe literature searches conducted by Adept which were the bases for the safety analysis in sections 6.2, 6.3 and 6.4. Within this description, please describe the databases searched, the search terms used, and the time period covered.

An extensive search of the world literature was initially conducted on February 5, 2019 in preparing this GRAS notice, and repeated on August 20, 2020 after submission of the GRAS

notice, and included the search terms as follows:

- Key search terms: polyvinyl alcohol, vinyl alcohol polymer, PVOH, 9002-89-5, methanol, methyl acetate, toxicokinetics, toxicity,
- Refining search terms (depending on output of key term search): absorption, distribution, metabolism, oral, ingestion, acute, subacute, subchronic, chronic, carcinogenicity, tumor promotion, genotoxicity, mutagenicity, clastogenicity, reproductive, developmental, irritation, hypersensitivity, allergy, neurotoxicity

The key search engines used included:

- PubMed (http://www.ncbi.nlm.nih.gov/pubmed)
- Toxnet (https://www.nlm.nih.gov/toxnet/index.html; includes HSDB, Toxline, ChemID Plus, and DART in Toxnet)
- ECHA (European Chemicals Agency – REACH dossiers) (https://echa.europa.eu/information-on-chemicals/registered-substances)

Other data sources searched for the key terms poly vinyl alcohol and/or 900-89-5 were:

- Cosmetic Ingredient Review (CIR) (https://www.cir-safety.org/ingredients)
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) (http://www.ecetoc.org/)
- eCFR (https://www.ecfr.gov/cgi-bin/ECFR?page=browse)
- EFSA Opinions (http://www.efsa.europa.eu/en/publications)
- FAO (Food and Agriculture Organization of the United Nations) (http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/)
- Google Scholar (https://scholar.google.com/)
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- International Programme on Chemical Safety (http://www.inchem.org/#)
- IUCLID (International Uniform Chemical Information Database) - https://iuclid6.echa.europa.eu/search
- NICNAS (Australian National Industrial Chemical Notification and Assessment Scheme) (https://www.industrialchemicals.gov.au/)
- NIOSH (National Institute for Occupational Safety and Health) (https://www.cdc.gov/niosh/topics/chemical.html)
- NTIS (National Technical Information Service) (http://www.ntis.gov/)
- NTP (National Toxicology Program) (https://ntp.niehs.nih.gov/)
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets) (https://hpvchemicals.oecd.org/ui/Search.aspx)
- SCCS (Scientific Committee for Consumer Safety) opinions: (http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm)
- SCOGS DB (https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=SCOGS
- Substances Added to Foods (https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=FoodSubstances)

7. A publication (i.e., "Sanders and Matthews (2009)) cited in the discussion of ADME (section 6.2.1, page 18) is not included in the reference list (section 7.1). Please provide a full

citation of this reference or give appropriate clarification.

The full citation is as follows: Sanders, J.M., Matthews, H.B. 1990. Vaginal absorption of polyvinyl alcohol in Fischer 344 rats. Hum Exp Toxicol 9: 71-77. We will be happy to provide a revised list of references, to include the citation for Sanders (1990), if it would be helpful.

8. On page 20, Adept concludes that the absence of carcinogenic activity reported in an NTP bioassay with intra-vaginal exposure to polyvinyl alcohol "indicates that polyvinyl alcohol is not carcinogenic [and] does not pose a carcinogenic risk from dietary exposures to this ingredient." Please provide a brief narrative to explain the basis of Adept's extrapolation from one route of exposure (intra-vaginal) to another (oral) with toxicokinetic information, such as the low oral absorption elaborated in Section 6.2.1.

In the published literature, no chronic toxicity or carcinogenicity studies were found following oral administration of polyvinyl alcohol. In a well-designed 2-year National Toxicology Program study (NTP; 1998) no treatment related neoplasms or nonneoplastic lesions were found in the reproductive system or other internal or external organs of female B6C3F1 mice receiving 20 µl 25% aqueous PVOH/day 5 days/week intravaginally for 2 years. The only clinical finding observed in this study was vaginal irritation. NTP concluded that there was no evidence that the low-viscosity PVOH (molecular weight approximately 24,000) has carcinogenic activity in this study.

As noted by NTP (1998), PVOH is used in surgical drapes, towels, and gauze sponges; protective gloves; cosmetic formulations; topical ophthalmic preparations; plastic sponge implants for reconstructive surgery, and intravaginal contraceptive foam and film. Furthermore, PVOH is used with magnesium sulfate to dilate the cervix of women prior to induction of labor. Hundreds of thousands of women in the United States use an intravaginal product containing PVOH each year. The FDA nominated low-viscosity polyvinyl alcohol for a 2-year study because of concern about the lack of information about the long-term toxic and carcinogenic effects by the intravaginal route.

The results of the NTP (1998) study are consistent with the observations from oral exposure studies demonstrating that PVOH is not absorbed systemically through the mucosa of the gastrointestinal tract and with the absence of genotoxicity observed in the genotoxicity tests of PVOH. Specifically, negligible absorption of PVOH through the vaginal mucosal surface, which is inferred from the demonstrated absence of absorption of PVOH through the mucosa of the gastrointestinal tract in oral studies, helps to explain the absence of any exposure-related lesions of the internal organs of the treated animals in the NTP study. Furthermore, the absence of neoplastic lesions in the internal and external organs of the intra-vaginally exposed mice, including on the directly exposed vaginal mucosal surface, is consistent with the lack of genotoxicity demonstrated in genotoxicity tests.

Based on the low absorption rate of polyvinyl alcohol through the mucosa of the gastrointestinal tract (discussed in Part 6.2.1.), the absence of genotoxicity concerns (discussed in Part 6.2.4.), and the results of the NTP study showing no neoplastic lesions in the internal and external organs of the intra-vaginally exposed mice, including on the *directly exposed* vaginal mucosal surface, Adept concludes there is no evidence that polyvinyl alcohol is carcinogenic and that polyvinyl does not pose a carcinogenic risk from dietary exposures.

If it would be helpful, we will be happy to provide a new safety narrative to replace the existing Part 6.2.5 with the more clear discussion above.

If you or Adept have any questions about the items that require clarification, please let me know. FDA respectfully requests a response within 10 business days. If unable to complete the response within that timeframe, please contact me. Thank you.

Sincerely,
Paulette Gaynor

Paulette M. Gaynor, Ph.D.
Senior Policy Advisor

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety, Division of Food Ingredients
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2.3 Specifications for food-grade PVOH

Food grade specifications for the PVOH used in the preparation of post-slaughter rectal plugs have been established by Adept and are presented in Table 1. These specifications comply with those in the Food Chemicals Codex (FCC 11th Edition, Third Supplement). The chemical and physical characteristics of PVOH have also been reviewed in several other national and international official monographs, including the United States Pharmacopeia (USP, 2004) and the JECFA Monographs 4 (2007). Analytical results of multiple independently produced, representative batches (Appendix I) demonstrate that the PVOH consistently meets the specifications.

Table 1. Specifications for PVOH

Parameter	**Characteristics**	**Reference/Test Methodology**
Description	Translucent, white or cream-colored granular powder	Visual inspection
Identification		
Color reaction A	Blue color	FCC
Color reaction B	Dark red to blue color	FCC
Precipitation reaction	White turbid precipitate	FCC
Infrared absorption	Pass (*i.e.*, same maxima at the same wavelengths as reference standard)	FCC
Specific tests		
Acid value	NMT 3	FCC
Ester value	Between 125 and 153 mg KOH/g	FCC
Degree of hydrolysis	Between 86.5 and 89.0%	FCC
Loss on drying	NMT 5%	FCC
pH	5.0 - 6.5	FCC
Particle size	NLT 99.0% material passes through (100-mesh sieve; sieved for 30 minutes)	FCC
Residue on ignition	NMT 1%	FCC
Viscosity	4.8–5.8 mPa·s (4% aqueous solution at 20°C)	FCC
Water insoluble substances	NMT 0.1%	FCC
Heavy metals		
Lead	NMT 2 ppm	ICP-MS
Organic impurities		
Methanol	NMT 1%	FCC
Methyl acetate	NMT 1%	FCC

NMT = Not more than;

NLT = Not less than;

ICP-MS = Inductively coupled plasma – mass spectrometry.

From:	Drozen, Melvin S.
To:	Gaynor, Paulette M
Cc:	Alsobrook, Lisa P.
Subject:	GRN 927--Response to FDA and FSIS
Date:	Wednesday, December 9, 2020 11:20:37 AM
Attachments:	GRN 927 (response to 11-2-2020 FDA email).pdf USDA response letter (11-2-2020 LPDS request).pdf Adept Soluble Two Flange Plug Test.docx ECHA 2008.pdf JECFA 2004.pdf Medical Device Tubing_ Polymer Solution Casting vs. Extrusion.pdf Ollari & Conti, Fatend Flushing System.pdf

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Dear Dr. Gaynor,

This email provides the attached responses for FDA and USDA/FSIS/LPDS (LPDS) which your November 2, 2020 email below asks that we send to you for dispersal to the teams. For ease of reference, we have also attached PDFs of the material that is cited in our responses. Because our response to LPDS references our response to FDA, we trust that you will provide both letters and all attachments to LPDS.

Please let us know if FDA or USDA has any further questions.

Sincerely,

Mel Drozen and Lisa Alsobrook.

From: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Sent: Monday, November 2, 2020 3:45 PM
To: Drozen, Melvin S. <Drozen@khlaw.com>
Subject: GRN 927 - topics for FDA and FSIS

Dear Mr. Drozen,

This email follows up on the October 30, 2020, phone conversation with FDA staff and FSIS staff.

FDA had asked for data to support the statement that residual vinyl acetate in the polyvinyl alcohol (PVOH) is not detected at the limit of detection of the method of 1 ppm (page 7 of the notice). In the amendment dated September 24, 2020, the notifier corrected the level of detection (LOD) for vinyl acetate and provided an exposure estimate~~s~~ for vinyl acetate based on the revised LOD. FDA is seeking clarification as to the appropriateness of the assumptions used in the exposure estimation and the relevancy of that exposure estimate given the manufacturing process for the PVOH that is described in the notice (page 7 of the notice) and the chemical properties of vinyl acetate; please provide a scientific narrative indicating the level of residual vinyl acetate that would be expected to be present in the PVOH.

FSIS has asked FDA to transmit the attached document concerning residual PVOH. FSIS has also asked that FDA pass along that one of the FSIS staff on the phone conversation was able confer with

a colleague with expertise in pork slaughter plants who informed them that plugs may be in place for up to 8 minutes in a typical high speed operation. In addition to the document, FSIS asked FDA to let you know that if you opt to correlate contact time with the dissolution of plug in aqueous solution in order to calculate a more accurate estimate of any potential residue, you should use 8 minutes rather than a minute or less as mentioned on the call.

Thank you in advance. Please send the responses to me, and I will convey to our FDA team and to FSIS.

Sincerely,
Paulette Gaynor

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December 9, 2020

Via Electronic Mail

Paulette M. Gaynor, Ph.D.
Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Campus Drive
College Park, MD 20740

Re: Clarification Regarding Polyvinyl Alcohol; Adept Limited; GRN 927

Dear Dr. Gaynor:

We are writing on behalf of our client, Adept Limited (Adept), to follow up on our October 30 telephone discussion with FDA staff, and your November 2, 2020 email. Specifically, we wish to clarify that no residual vinyl acetate is expected to be present in the polyvinyl alcohol (PVOH) that is the subject of Adept's Generally Recognized as Safe (GRAS) Notice, GRN 927, which we submitted on March 27, 2020.

GRN 927 concerns the use of PVOH as a component of water-soluble plugs for use in abattoirs by inserting a plug into the anus of a slaughtered sheep, lamb, or hog for the purpose of blocking the exit of fecal matter and preventing contamination of the carcass with intestinal contents until the plug is removed during cleaning of the contacted meat. Specifically, in response to your request for clarification,[1] we have provided a scientific narrative in Section I, below, regarding the manufacturing and processing steps which ensure that residual vinyl acetate is not an expected impurity in the PVOH. Additionally, in further support of Adept's conclusion that PVOH is GRAS when used as intended, we have provided in Section II, below, the results of testing conducted by Adept to demonstrate the maximum extent of potential dissolution of the plug prior to removal. Furthermore, we have explained that the PVOH will not be able to form a film under the conditions of use and, thus, any PVOH (and its constituents) dissolved from the

[1] *See* November 2, 2020 email from P. Gaynor of FDA to M. Drozen of Keller and Heckman.

plug will be completely removed by routine washing steps during the harvesting of meat and other products.

I. Vinyl Acetate

FDA has questioned the relevancy of an estimate that we calculated for dietary exposure to vinyl acetate monomer (VAM) from the use of PVOH in the noted application.[2] A theoretical dietary exposure estimate was provided in an abundance of caution, to demonstrate that the intended use of PVOH is GRAS, even under the unrealistically exaggerated assumption that VAM could be present at the limit of detection (LOD) achievable by the analytical method used to analyze the PVOH for theoretical impurities, even though there actually is no reasonable expectation that VAM is present in the PVOH.[3] In this regard, a statement in GRN 927 indicating that residual VAM was not detected in the PVOH is misleading because it implies, incorrectly, that VAM could potentially be present. Specifically, testing to confirm the absence of VAM was unwarranted in the first place because, as discussed in further detail below, VAM is not an expected impurity in PVOH. A dietary exposure estimate of VAM, therefore, is not relevant to Adept's GRAS conclusion.

A review of the manufacturing steps confirms that VAM is not realistically expected to be present in PVOH. To produce PVOH, as you know, VAM must first be polymerized to form a polyvinyl acetate polymer. While VAM is an expected impurity in the polyvinyl acetate, the saponification process used to convert polyvinyl acetate into PVOH will result in hydrolysis of any residual VAM. In fact, a Summary Risk Assessment Report for Vinyl Acetate prepared by the German Federal Institute for Occupational Safety and Health notes that, during the production of PVOH, "[A]long with saponification (alkaline hydrolysis of fatty acid esters) of the acetyl moieties of polyvinyl acetate, monomer residual are getting eliminated as well." The report further states:

> "As polyvinyl alcohol is produced by transesterification (saponification) of vinyl acetate (co)polymers, residual vinyl acetate monomer does not occur in polyvinyl alcohol and in polymer derived from polyvinyl alcohol. Hence the manufacturing of polyvinyl alcohol is not relevant in the context of residual monomer content."[4]

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[2] *Id.*

[3] *See* September 24, 2020 email from M. Drozen to P. Gaynor.

[4] *See* Vinyl Acetate, CASRN 108-05-4, Summary Risk Assessment Report (2008), https://echa.europa.eu/documents/10162/6434698/orats_summary_vinylacetate_en.pdf. *See* page 7-8.

In this regard, the conclusions summarized by the German Authorities, as well as the absence of specifications for VAM among the impurities for which testing and acceptance criteria are specified in the Food Chemicals Codex (FCC) monograph for polyvinyl alcohol, confirms the logic leading to our conclusion from the analysis of the PVOH manufacturing process.

II. Complete Removal of PVOH Residue

No dietary exposure to PVOH or its constituents is expected because less than 1% (by weight) of the plug will dissolve under the intended conditions of use and any low levels of PVOH that do dissolve will be removed from the animal tissues during the extensive washing steps that accompany breakdown of the animal. To be conservative, however, potential dietary exposure to PVOH was estimated in Adept's GRN 927 by assuming that 1% of the plug remains on the inside surface of the tissue ("bung portion") and 99% is washed away under the intended conditions of use (*see* page 11). Subsequently, Adept tested the dissolution of the plugs with time under simulated use conditions. The results demonstrate, as discussed in detail below, that no more than approximately 1% of the plug will dissolve while in use (*i.e.*, in contact with animal tissues). Further, as also discussed below, based on the properties of the plug and the conditions of use, this quantum of dissolved material will be easily washed away during routine processing and have no potential to form a film and/or to be present on processed products post-slaughter.

A. Dissolution Study

As you know, the United States Department of Agriculture's (USDA) Food Safety Inspection Service (FSIS) requested quantitative data to support the assumption in GRN 927 that 1% of the plug remains on each casing. Because no standardized test methods are available for the quantification of PVOH when used under such circumstances,[5] Adept undertook a study to quantify the weight of the plug that could potentially be lost (*i.e.*, dissolve) under the intended conditions of use. A copy of the study is attached.[6]

Based on experience in other countries, the plug is known to remain intact until it is removed during washing. Thus, very little, if any, PVOH could remain inside the anal canal, rectum or intestines, much less in a fully processed sausage casing produced from these tissues.

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[5] Joint FAO/WHO Expert Committee on Food Additives (JECFA), Polyvinyl Alcohol (PVA), Chemical and Technical Assessment, 61st JECFA (2004) *available at* http://www.fao.org/fileadmin/templates/agns/pdf/jecfa/cta/61/PVA.pdf. *See* page 2.

[6] *See* Adept Soluble Two Flange Plug – Dissolution Over Time Inside Pig Intestine.

Ideally, a study comparing the weight of the plug before and after use would be conducted in an abattoir under actual processing conditions. Due to COVID-19 restrictions, however, it was not possible for Adept to arrange this type of experiment. Therefore, the actual use of the plug (which is inserted immediately post-slaughter into the anal canal/rectum of the animal) was simulated by inserting the plugs into wetted hog intestines 20 cm in length and then submerging the plugged samples in warm (38°C) water. Weight loss of the plugs (inside the wetted intestines) after submersion in water for 8 minutes, which represents the maximum duration that plugs may be in place in a typical high-speed hog processing operation,[7] is presented in Table 1 below.

Table 1. Weight loss of plug exposed to simulated conditions for 8 minutes.

Sample	Weight-before (g)	Weight-after (g)	Weight loss (g)	Weight loss (wt.%)
1	6.65	6.6	0.05	0.75
2	6.66	6.6	0.06	0.90
3	6.68	6.61	0.07	1.05
			Average	**0.90**

Under the test conditions of this dissolution study, which are at least as severe as the actual conditions of use of the plugs, weight loss of the plug on average was 0.90%.

B. Removal of PVOH During Meat Processing

Based on the dissolution study discussed above, we have assumed that the plug may partially dissolve during use. Because dissolved PVOH will remain in solution, however, deposition onto the inner surface of the bung/intestines of slaughtered animals will not occur. Even if low levels of deposition of PVOH could occur, as a theoretical matter, consideration of the film-forming properties of PVOH, as discussed below, confirms that the dissolved material would not form a coherent film and will be easily removed by flushing with water in any case.

While it is widely known that "solution cast films" can be formed from PVOH, any dissolved plug components are not expected to re-form to produce a film during the processing of the bung/intestines. Regardless of whether the dissolved plug components could possibly form films under optimum solution casting conditions (as opposed to the intended conditions of use), film-formation will certainly not occur under the high-moisture conditions of the

[7] *See* your November 2, 2020 email (conveying information from a subject matter expert from FSIS).

bung/intestines because Adept's plugs are formulated to dissolve in water over time, not to form films.

Although the bung/intestines somewhat resemble the tubular shape of an inner-diameter mold that could possibly be used in some polymer solution casting methods,[8] the presence of moisture, fecal matter, intestinal mucous, as well as the other constituents of the plug, will dilute the polymer concentration and, together with the moisture of the environment, will prevent film formation. That is to say that, even if a polymer solution comprising plug residue combined with fecal matter and mucous, with the inside the surface of bung/intestinal tissue serving as a mold, could theoretically be amenable to film formation by casting, a film cannot form when the plug is used as intended because no curing or drying can occur under the conditions of the use of the plugs. Specifically, rather than being dried, as is necessary for film formation, the plug and any dissolved PVOH inside the intestines from a slaughtered animal remain moist while the plug is in place and are then completely wetted when the plug is removed and the intestines then washed extensively thereafter. The extensive washing procedures would transport any dissolved PVOH away from the intestinal tissues rather than permitting deposition and potential film formation on the tissues.

Based on the foregoing discussion, film formation is not reasonably expected and "loose" PVOH will be readily washed away by any process sufficient to remove fecal matter (as required for the tissues to be considered clean for use in human food products). In this regard, the cleaning process for bung portions and intestines used to produce sausage casings is so water intensive that there is no reasonable expectation of finding detectable PVOH residue on or in the tissues, much less in the casings produced from the tissues. For example, the technical specification for water consumption for an automatic hog-bung (fat-end) flushing system that can process 1,250 hogs per hour (20 to 21 hogs per minute) is 100 liters/minute.[9] Thus, at least 4.7 liters of water per hog would be used by this equipment to flush the bung, compared to about 0.05 to 0.07 grams of dissolved residue of the plug, which is formulated to dissolve in water.

The information provided above, including data demonstrating that, at most, approximately 0.9% of the plug, on average, could dissolve while in contact with the tissue during use, the dissolved constituents of the plugs lack the capacity to form films under the conditions of use, and the copious volumes of water used routinely to clean the anal canal,

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[8] The article *Medical Device Tubing: Polymer Solution Casting vs. Extrusion* discusses how an inner-diameter mold may be immersed in a polymer solution to form a thin film. See https://www.mddionline.com/medical-device-tubing-polymer-solution-casting-vs-extrusion.

[9] *See* Ollari and Conti, Automatic hog bung (fatend) flushing system, MOD.VGA1250 http://www.ollarieconti.it/index.php?option=com_content&view=article&id=222&Itemid=474&lang=en.

rectum and intestines of the animals after the use of the plugs, supports the conclusion that no detectable residue of PVOH can reasonably be expected to be present in foods produced from these tissues.

* * *

We hope and trust that the information above responds fully to FDA's questions regarding Adept's GRN 927. We look forward to the Agency's continued review of the Notice and we would be happy to provide you with any further information you may need.

Sincerely,

Melvin S. Drozen

Attachment

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December 9, 2020

Via Electronic Mail

Labeling and Program Delivery Staff (LPDS)
Food Safety Inspection Service (FSIS)
United States Department of Agriculture (USDA)
Patriots Plaza III
1400 Independence Avenue, SW
Washington, DC 20250

Re: Clarification Regarding Polyvinyl Alcohol; Adept Limited; GRN 927

Dear LPDS:

We are writing on behalf of our client, Adept Limited (Adept), to follow up on our October 30 telephone discussion with the Labeling and Program Delivery Staff (LPDS) of the United States Department of Agriculture's (USDA) Food Safety Inspection Service (FSIS) regarding Adept's Generally Recognized as Safe (GRAS) Notice, GRN 927, for the use of polyvinyl alcohol (PVOH) as a component of water-soluble plugs to be inserted into the anus of a slaughtered sheep, lamb, or hog for the purpose of blocking the exit of fecal matter and preventing contamination of the carcass with intestinal contents until the plug is removed during cleaning of the contacted meat. The LPDS explained in our teleconference, and in a letter sent to us in a November 2, 2020 email from the U.S. Food and Drug Administration (FDA),[1] that FSIS requires further information to determine whether PVOH meets the definition of a processing aid through 21 C.F.R. § 101.100(a)(3)(ii) when used as intended.

Adept's plugs are not formulated for film-formation but instead are specifically designed to dissolve in water over time. In this regard, data and scientific references provided in our attached December 9, 2020 letter to FDA demonstrate that less than 1% of the plug may dissolve prior to removal,[2] and once dissolved, PVOH originating from Adept's water-soluble plug will

[1] *See* November 2, 2020 email from P. Gaynor of FDA to M. Drozen of Keller and Heckman.

[2] *See* December 9, 2020 letter at Part II.A (Dissolution Study).

not form a coherent film or be deposited onto the inner surface of the bung/intestines of slaughtered animals.[3]

* * *

We hope and trust that the information provided in the attached letter, as described above, will enable the LPDS to conclude that PVOH meets the definition of a processing aid under 21 C.F.R. § 101.100(a)(3)(ii)(a), "Substances that are added to a food during the processing of such food but are removed in some manner from the food before it is packaged in its finished form." We look forward to the Agency's continued review of the Notice and we would be happy to provide you with any further information you may need.

Sincerely,

Melvin S. Drozen

Attachments

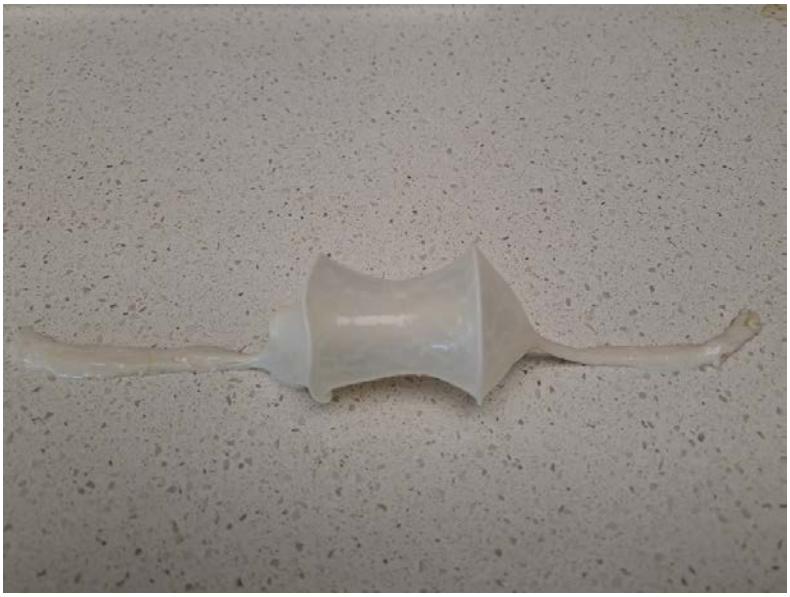
[3] *See* December 9, 2020 letter at Part II.B (Removal of PVOH During Meat Processing).

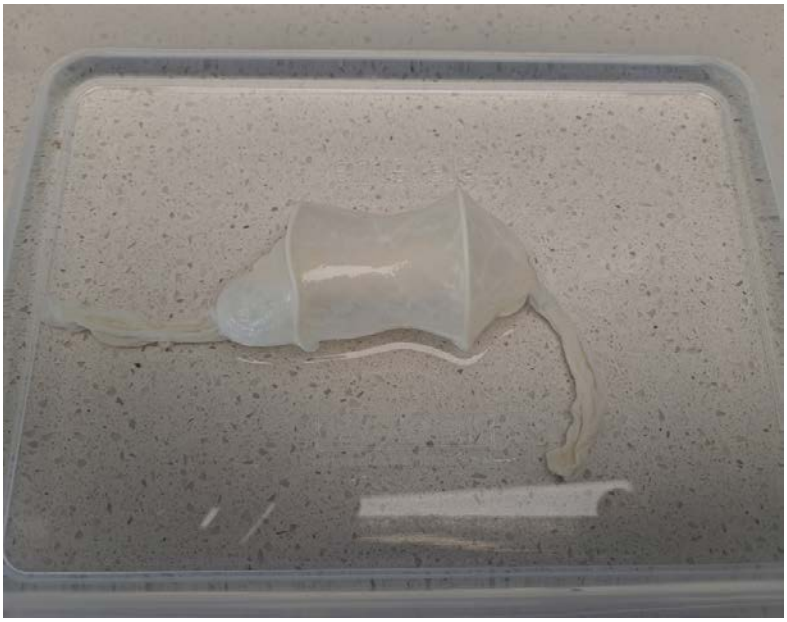
Adept Soluble Two Flange Plug – Dissolution over time inside Pig Intestine

The below test was conducted to determine the amount of ADSOL soluble material that is lost from an Adept Soluble Plug while inserted in a Pig Intestine. This is to simulate the amount of material lost when inserted in the Pig rectum during processing.

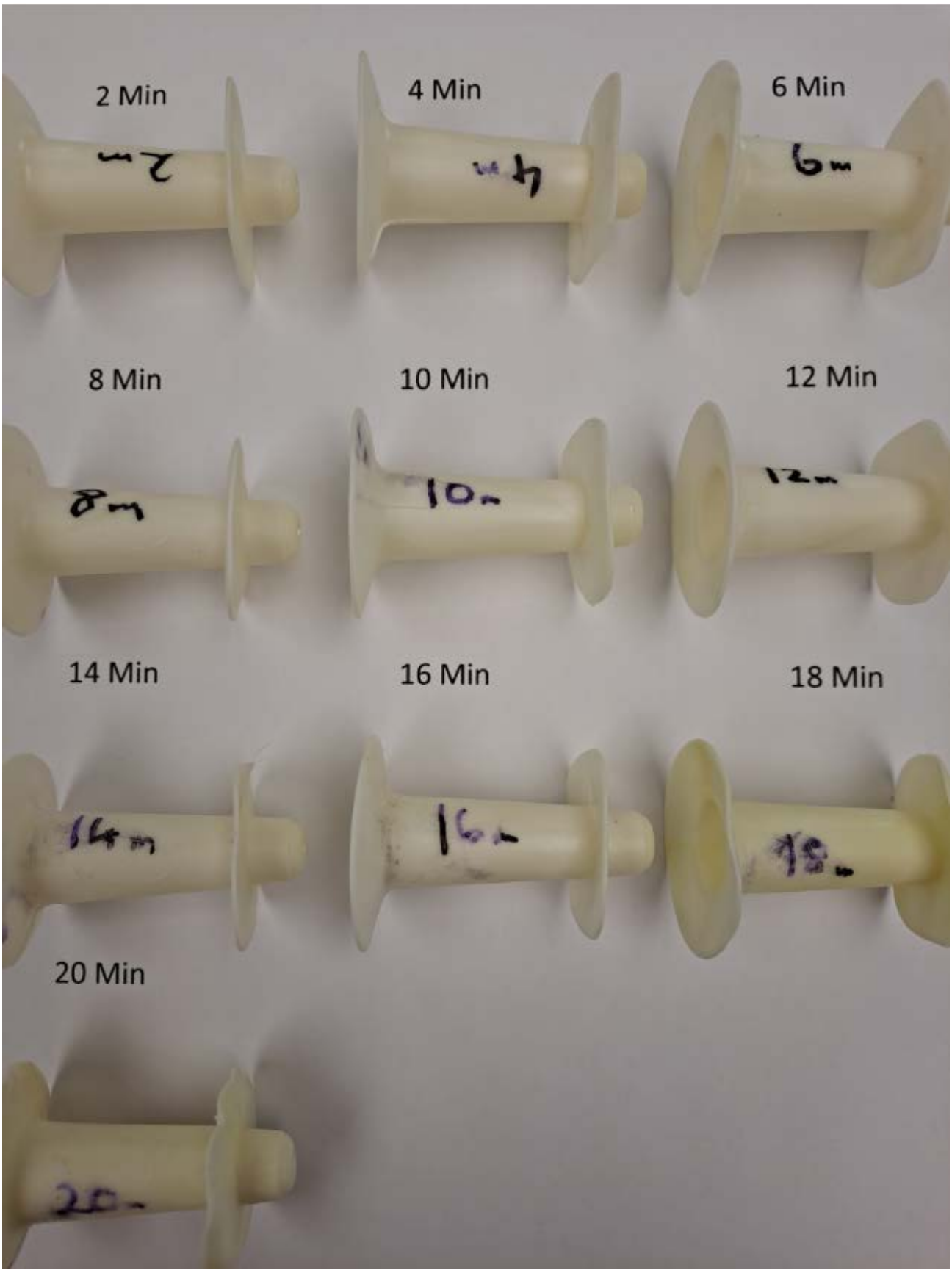
Plug Samples:
Plugs were dried in a descant drier (Dew point – 50, 80°C) for 20 hours directly after manufacture to ensure all moisture was removed prior to the test. Each plug was then weighed after drying as a base line.

Test Method:
A 200mm piece of Pig Intestine was soaked in warm distilled water (temperature of 38°C) for 5 minutes. The intestine was then flushed with warm distilled water (note it was not dried). Each plug was then inserted into the pig intestine and placed in a container into a bath of warm water (temperature of 38°C) and the lid then sealed for the measured amount of time.





The plug was then cut out of the intestine and placed in a descant drier (Dew point – 50, 80°C) for 20 hours to remove all moisture content before being weighed again to measure the amount of material that had been lost.



Results:

Sample Batch 1

Time	Initial Weight	Final Weight	Material Loss
Mins	(20 Hrs Drying)	(20 Hrs Drying)	(g)
2	6.64	6.61	0.03
4	6.65	6.61	0.04
6	6.66	6.6	0.06
8	6.65	6.6	0.05
10	6.64	6.59	0.05
12	6.66	6.56	0.1
14	6.67	6.56	0.11
16	6.65	6.55	0.1
18	6.69	6.57	0.12
20	6.66	6.48	0.14

Sample Batch 2

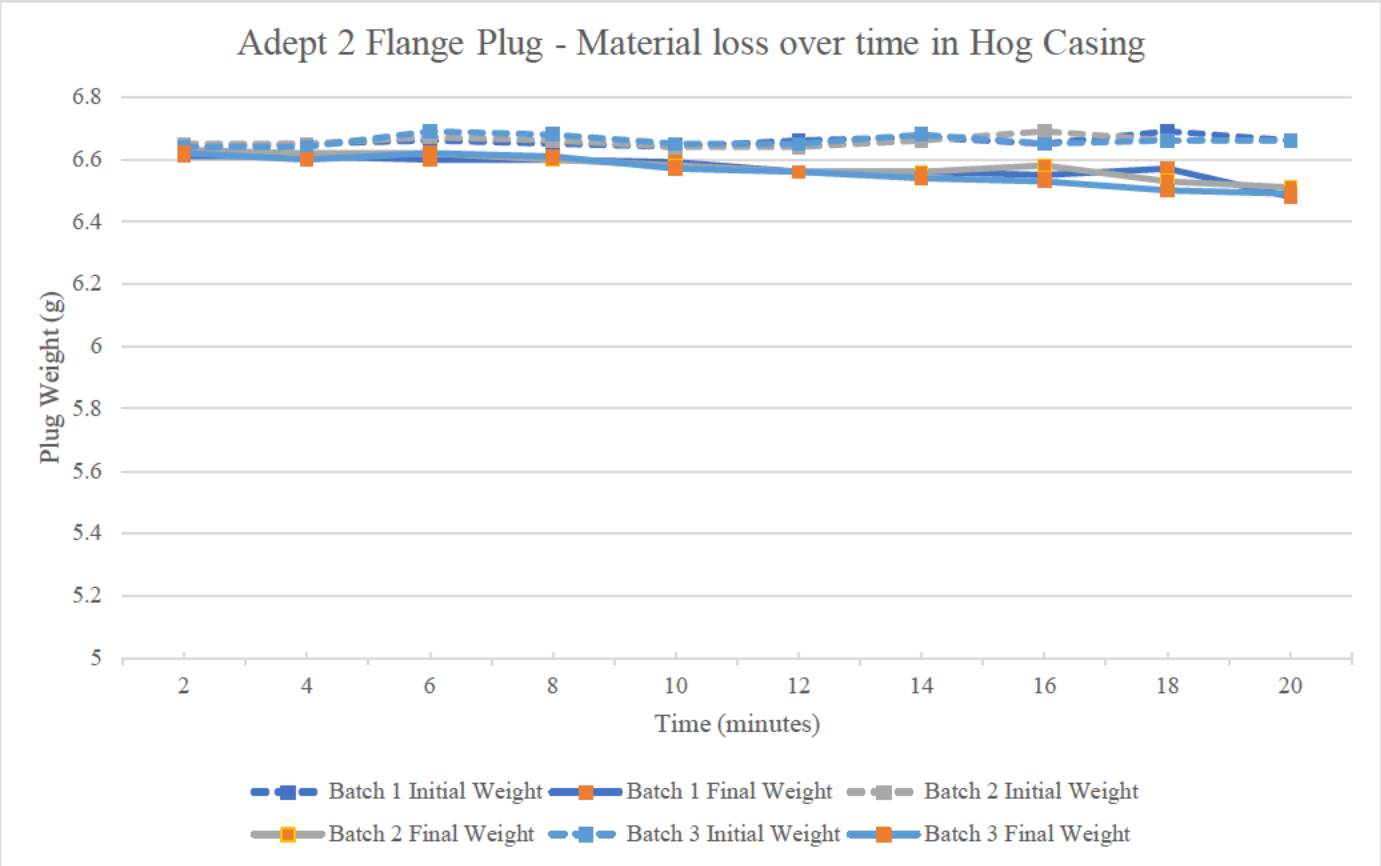
Time	Initial Weight	Final Weight	Material Loss
Mins	(20 Hrs Drying)	(20 Hrs Drying)	(g)
2	6.65	6.63	0.02
4	6.65	6.62	0.03
6	6.67	6.62	0.05
8	6.66	6.6	0.06
10	6.64	6.58	0.06
12	6.64	6.56	0.08
14	6.66	6.56	0.1
16	6.69	6.58	0.11
18	6.66	6.53	0.13
20	6.66	6.51	0.15

Sample Batch 3

Time	Initial Weight	Final Weight	Material Loss
Mins	(20 Hrs Drying)	(20 Hrs Drying)	(g)
2	6.64	6.62	0.02
4	6.64	6.6	0.04
6	6.69	6.62	0.07
8	6.68	6.61	0.07
10	6.65	6.57	0.08
12	6.65	6.56	0.09
14	6.68	6.54	0.14
16	6.65	6.53	0.12
18	6.66	6.5	0.16
20	6.66	6.49	0.17

Average

Time	Average material loss
Mins	(g)
2	0.023
4	0.037
6	0.060
8	0.060
10	0.063
12	0.090
14	0.117
16	0.110
18	0.137
20	0.153



Medical Device Tubing: Polymer Solution Casting vs. Extrusion

While countless tubes are extruded or injection molded each year, these manufacturing techniques are neither the most optimal nor the most cost-effective methods available to medical device manufacturers. At least that's the word from Avalon Laboratories (Rancho Dominguez, CA), whose polymer solution casting technology can be used to manufacture flexible plastic components without resorting to conventional extrusion or injection-molding processes.

A coil-reinforced catheter with introducer is manufactured using Avalon Laboratories' polymer solution casting technology.

Polymer solution casting begins with a mandrel or an inner-diameter mold that is carefully immersed into a tank of tightly controlled polymer solution, explains Michael Janish, Avalon Laboratories' president and CEO. Responding to a combination of thermal and frictional properties, the liquid plastic forms a thin layer around the mold, which is then extracted from the bath and cured. Once the first layer of the thin film has solidified adequately, other features can be added to the product, such as coiling, braiding, other types of metal reinforcements, and even imaging targets. Multiple casting steps can then be repeated to build up wall thicknesses, add additional lumens, and optimize column strength. After it is totally cured and solidified, the part is removed from the mold.

This casting technology, Janish says, was developed for the manufacture of cannulae, a subset of catheters that is typically used for directing blood flow. While it can be used for many other

applications, the method is commonly used to manufacture cannulae used in open-chest procedures to provide extracorporeal membrane oxygenation.

"This thin-film processing technology is unique because it can meld materials with different properties--including strength, durometer, color, and lubricity," Janish remarks. "For example, the first layer can be made out of a lubricious material to enable the passage of such medical devices as stents, while the outer layer can be composed of material that adds column strength. Alternatively, a layer can be made from materials offering a range of different cytotoxicity properties or lubricious

Janish. "Our mandrels and molds in most cases are axisymmetrical, meaning that they're made on a lathe and a grinder. While complicated extrusion die heads or tooling for such applications as inner lumens require the use of a mandrel in between the tooling, our process can create multiple lumens using piano wires and other axisymmetrical molds to create the additional lumens.

In typical extrusion processes, operators pour pellets into one end of a machine to melt and blend them into a gel. Then, the material is pushed through a die head, from which it emerges in the shape of tubing. "The problem with this method is that you usually can't perform many alterations," Janish notes. "The tubing is consistent from the distal to the proximal end--from the tip to the tail. And while you can vary the speed of the machine a little bit and perform bump extrusion to modify the inner or outer diameter, you can't vary the features of the tube very much." To form features, the tubing must be run through another machine to add such reinforcements as braiding or coiling, Janish adds. And in most cases, you have to take a piece of another extruded tube, place it over the top of the first tube, and then shrink the assembly together using a heat gun to create the final construction.

In the catheter-manufacturing space, the inner-diameter surface of a tube is often composed of a different material from the outer diameter surface. For example, because doctors are used to feeling their way through a catheter as they press a stent or other device through it, they frequently prefer that the inner liner be composed of PTFE. Avalon's technology enables users to mount an extruded

piece of PTFE or other material on a mandrel and then cast polymer on top of it. This process, Janish says, enables manufacturers to embed extruded components in their tubing. "If a multilumen part containing a polyimide lumen is needed to achieve such attributes as column strength, high pressure, or consistency at body temperature, we can embed a polyimide-extruded tube inside of our solution casting technology."

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The Value of a Molecular Diagnosis of Epilepsy

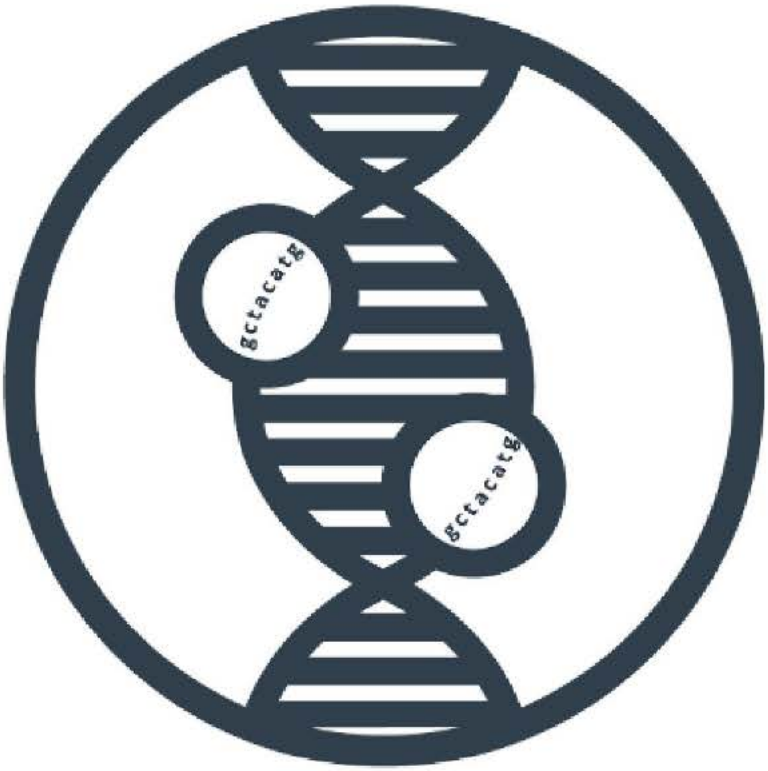

Image courtesy of Variantyx

Identifying the genetic cause of epilepsy using whole genome sequencing could lead to better disease management.

Holly Head, MS CGC | Nov 10, 2020

When discussing a diagnosis of epilepsy, advances in genetic testing are proving that it is indeed all about the details. Comprehensive genetic testing is making it possible to drill down into those details. When testing is based on whole genome sequencing (WGS) technology, it is possible to identify genetic changes, or variants, in the 370-plus seizure-associated genes found amongst the 20,000 or so genes within the human genome or, more importantly, the large number of variants located within or spanning those genes. A single-method approach for detecting multiple variant types from a single patient sample can more accurately lead to a diagnosis, resulting in more-tailored medical management and providing a better basis for improved long-term outcomes and family planning.

In the United States, epilepsy is the fourth most common neurological condition, surpassed only by migraine, stroke, and Alzheimer's disease. Each year, 150,000 people on average will develop epilepsy (48 out of 100,000) and its prevalence is currently estimated at around 2.2 million people (or 7.1 out of every 1,000 people). Epilepsy is a spectrum condition characterized by unpredictable seizures that can cause or co-occur with other health problems. There is a wide range of seizure types and the ability to control them varies from person-to-person, even within families. The cause of epilepsy is often unknown, but it is most often related to brain injury or genetics. However, the word epilepsy itself has nothing to do with the cause, severity, or type(s) of an individual's seizures.

Genetic seizure disorders span multiple classes. They can include specific syndromes in which a seizure is the only symptom as well as occur as part of broader neurodevelopmental conditions that present with additional features, such as intellectual disability. Seizures may also be present as a symptom of metabolic conditions and/or other disorders. Seizure disorders share symptoms (phenotypes) with many other conditions, which often make it difficult to determine the inheritance pattern from the family history. Causal variants may be inherited from a parent or simply show up new (de novo) in a person's DNA. In some cases, variants in multiple genes may together contribute to the clinical symptoms. Many different types of variants have been shown to cause seizure disorders.

This is why definitively diagnosing the genetic cause of epilepsy can be challenging. Traditionally, this is accomplished through multiple, sequential tests. This step-wise method typically begins with what is known as a "chromosomal microarray," which involves structural analysis of a person's chromosomes and checks to make sure there are no large imbalances (extra or missing pieces) that could cause epilepsy. If the microarray does not reveal a positive result, the next step is usually single-gene or multi-gene panel testing, depending on the specific nature of the individual's symptoms. If no causal variant is identified with those tests, the final step is exome testing, if the patient's insurance allows for multiple genetic tests. This results in a long process of repeated rounds of testing, with each individual round limited by the types of variants that can be detected, leaving gaps in variant coverage and detection, and therefore leaving gaps in the ability to properly diagnose a patient. That is because, as a general rule, microarray, panel, and exome tests individually do not perform well at detecting a broad spectrum of changes (variants) in genetic material.

Comprehensive testing based on WGS technology has the ability to detect a wide range of variant types not covered by traditional microarray, panel-based, or exome tests, as well as the ability to reanalyze patient data in the future without resequencing. Combining WGS's consistent,

variants and genes associated with genetic epilepsy. All of this is accomplished with a single blood draw (or saliva sample) and a turnaround time of six to eight weeks.

The ability to quickly establish a genetic cause of epilepsy utilizing WGS can provide the information necessary to control an individual's seizures as soon as possible. The longer a patient experiences uncontrolled seizures, the more likely they will suffer irreparable damage to the brain. Depending on their frequency and length, uncontrolled seizures can interfere with daily activities and can negatively impact someone's quality of life. The sooner that clinicians can identify an individual's cause of seizures and treat it appropriately, the better the prognosis for the long-term management of disease.

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The machine is suitable for the individual manual de-fatting by the worker, separation of the organs attached, automatic manure flushing and automatic cutting of the crown along with easy disposal of the waste product.

The Unit is composed of:

- A support structure in stainless steel
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- Mechanical/Automatic water injection system for the flushing
- Motorized circular blade to cut the rectums crown
- Motorized brush to remove the crown from the nozzles
- Automatic Self-Cleaning system for the chain
- Security Barriers along the unit
- The machine can be equipped with belts, chutes, pumps, pneumatic conveyors (link) for the transport of the product and waste
- The unit is shipped in section for easy installation
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Technical Characteristics:

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