Emerging Issues on Chemical and Drug Residues in Meat

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This paper addresses emerging drug and chemical residues of meat safety significance. The beef industry will continue to meet new challenges related to chemical residues. The events of September 11, 2001 have raised concerns about the possibility of economic terrorism in the United States. As far as meat safety is concerned, the potential for terrorists to contaminate livestock feeds with chemicals is real. Also, use of a dirty bomb may result in contamination of beef with radionucleides. The safety of meat derived from cattle that are exposed to weapons of mass destruction has not been a major concern in the past. As such, the veterinary professionals and the meat industry are ill-prepared to deal with meat safety issues related to use of chemical and radiological weapons because of gaps in data. The USDA has been concerned about drug and environmental chemical residues in meat and other livestock products. This is understandable because drugs and pesticides are widely used by the livestock industry to increase productivity of cattle and other livestock, and hence they are likely to be present in livestock products. Emphasis now needs to be placed on research that is likely to produce data to answer questions related to chemical weapons.

Another challenge facing the beef industry is the introduction of new drugs and pesticides. There is a continued drive by drug manufacturers to produce newer and more effective animal drugs, including antibiotics. The challenge of microbial drug resistance and the emergence of new infectious diseases are the driving force to produce newer more effective antibiotics. The same is true with pesticides. Pesticide manufacturers are always striving to produce newer classes of pesticides. The result is that the meat industry has to be aware of the potential for toxicity from the newer drugs and pesticides.

Experience from the diagnostic laboratory shows that old banned pesticides such as Toxaphene still continue to pose danger to the consumer. Toxaphene and other persistent chlorinated pesticides, which were banned in 1970's, continue to poison cattle in USA. Persistent environmental pollutants also continue to be a challenge in meat safety as recent cases of dioxin contamination in poultry have demonstrated. Although the meat industry was spared, the dioxin contamination incidents involving Ball clay in poultry in the USA and the Belgian dioxin poultry remind us that this could occur in beef cattle as well. Vigilance is therefore required to protect the public from persistent environmental pollutants that may contaminate meat. Human error has historically been a factor in some of the major food safety disasters that have occurred in this country. For example, the polybrominated biphenyl (PBB) disaster, which occurred in Michigan in the early 1970s, was caused by mistaking PBB fire retardant for magnesium oxide concentrate. Such unintentional accidents will likely continue to occur, especially at the farm level. Adequate steps need to be taken to ensure that contaminated beef does not reach the consumer. Most concern is with persistent organic chemicals, which are not readily metabolized in the body and have low acute toxicity such as dioxins, polychlorinated biphenyls (PCBs), PBBs, and dibenzofurans. These chemicals cause immunosuppression and cancer in livestock and consumers and their effects are not immediately recognized. Therefore, continued surveillance or monitoring of meat is necessary to detect the presence of these persistent chemical pollutants in meat and to protect consumers. A summary of current and emerging chemicals of meat safety concern follows.

Chemical Terrorism and Beef Safety

The list of potential chemical compounds that can be used by terrorists is long. However, the FBI has compiled a short list of the most likely compounds to be used by terrorists and these are shown in Table 1 below. This includes organophosphate and carbamate pesticides, heavy metals such as arsenic and mercury compounds, rat poisons, and herbicides among others. Others not on the list are radionucleides, which are likely to be released from dirty bombs. Most emphasis has been placed on the direct toxicity of these compounds in humans, but use of these chemicals will likely affect animals as well, including meat-producing animals. The major challenge is that there is no sufficient data on the risk analysis to determine the safety of meat

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from animals exposed to most of these chemicals. Research is needed to answer risk analysis issues related to these chemicals should terrorists use them.

Clenbuterol

Violative levels of animal drugs can have adverse health effects in consumers. A vigilant chemical residue prevention program is essential in preventing illnesses and fostering the prudent use of drugs in animals that enter the human food supply. Clenbuterol is a β-2 selective bronchodilator drug which was the most popular illegal drug used in food producing animals in 1990s. The drug is approved for use in veterinary medicine in Europe but not in the USA. Meat from clenbuterol-treated animals has caused illness and death in people. For example, in Spain more than 130 people became sick following consumption of liver containing 0.16-0.30 ppm clenbuterol residues. Muscle tremors, heart palpitations, fever, nausea and vomiting were some of the clinical signs exhibited by affected patients. Other episodes of clenbuterol poisoning have been reported in France (1991), Spain (1994), and Italy (1995 and 1996). One of these (Italy 1995) involved ingestion of beef fillet containing more than 0.5 ppm clenbuterol.

Synthetic Growth Hormones

Sex steroid hormones and synthetic derivatives are used to enhance growth and for herd management such as estrous synchronization. There are six hormonal drugs approved for use in the USA. These include three natural hormones 17β-estradiol, testosterone, and progesterone, and three synthetic hormones trenbolone acetate, melengeterol acetate and zearanol. Meat from cattle treated with any of the six hormones cannot be exported to the European Union. There are unresolved issues concerning health effects of hormonal residues in humans. Acceptable levels of residues in edible tissues are an incremental exposure of 1% of the amount of sex steroids produced through daily *de novo* synthesis in the lowest producing segment of the population (prepubescent boys for estrogen and progesterone and prepubescent girls for testosterone). The three natural hormones approved for use as growth promoters meet this guideline and require no withdrawal period.

Related to growth hormones but currently unregulated are environmental endocrine disrupting chemicals. Research is needed to determine if environmental endocrine disrupting chemicals can be found in meat and at what levels. Phytoestrogens for example, have similar physiological effects as growth hormones that are used as growth promoters by the beef industry. A similar level of concern can be expected of the natural environmental estrogens in the future as the natural or synthetic steroid hormones discussed above. The meat industry should be prepared to address concerns in the area of endocrine disruptors in the future.

Persistent Environmental Pollutants

The persistent environmental pollutants of concern are the polybrominated biphenyls (PBBs), polychlorinated biphenyls (PCBs) and dioxins. These are industrial compounds and the concern is accidental contamination of livestock through feed by these chemicals. They are also the kind of chemicals likely to be used by economic terrorists. The contamination of animal feed by PBBs, which occurred in Michigan in the early 1970s, is by far the largest food contamination disaster in US history. Recent poultry feed contamination by dioxins from ball clay in the USA and the Belgian feed contamination by dioxins remind the meat and livestock industry to remain vigilant. The agricultural industry should invest in the infrastructure capable of detecting these chemicals in beef and other livestock products. The residue limit for PCBs in fat is 3 ppm. The interim regulatory level of concern for dioxins in animals and animal products is 1 ppt TCDD. This interim level is not a health-based safe level as this is yet to be established. More research is needed in the risk assessment arena to determine a safe level of these chemicals in meat.

Health Effects of Drug and Chemical Residues in Humans

The health effects of chemical residues will be discussed in order to emphasize why it is important to ensure that meat is "free" of these compounds. The three most common health consequences of exposure to chemical and drug residues are allergenicity, pharmacological response, and carcinogenesis. Allergies are caused by the immune system reacting with chemical residues. In humans, penicillin and streptomycin are the most likely to cause allergic reactions. However, allergenicity has been reported in response to aminoglycosides, sulfonamides and tetracyclines. Allergic reactions are manifest as rashes, anaphylactic shock, asthma or fever.

An excellent example of a drug residue that causes a predictable pharmacologic response is clenbuterol. This is a β-adrenergic agonist, which is an effective bronchodilator in many species, including cattle. It has high binding affinity and specificity for β1 and β2 adrenergic receptors. Toxicity in humans is characterized by muscle tremors, heart palpitations, muscle pain, chills and vomiting.

Drugs approved for animal use are not of concern as far as carcinogenesis is concerned because a drug that causes cancer either as a parent drug or as drug metabolite will not be approved for use in food animals. The major concern regarding carcinogenesis is environmental chemical pollutants such as dioxins. Cancer may result either from immunosuppression or direct chemical interaction between chemical and its metabolites with DNA. However, it is very difficult to pinpoint a cause-effect relationship between chemicals and cancer because of the long period between exposure and the time cancer develops. Theoretically, any amount of carcinogen can lead to cancer. Other concerns with chemical residues include teratogenesis i.e. abnormal fetal development. In the USA about 7% of infants are borne with birth defects and it is predicted that about 6% of these birth defects are caused by chemicals and drugs.

Table 1. Highly toxic pesticides and OP nerve agents judged likely to be used by terrorists or for malicious intent.

Nerve agent or pesticide	Common trade name or synonym	CAS No.	Terrorist (T) or Malicious (M) use
Organophosphate nerve gas:			
sarin (GB)		107-44-8	T
tabun (GA)		77-81-6	T
soman (GD)		96-64-0	T
GF		329-99-7	T
VX		50782-69-9	T
OP insecticides:			
ethyl parathion*	Parathion	56-38-2	M
fonofos*	Dyfonate	944-22-9	
mevinphos*	Phosdrin	7786-34-7	
monocrotophos*	Azodrin	6923-22-4	
TEPP* (tetraethyl diphosphate)	- -	107-49-3	
azinphosmethyl	Guthion	86-50-0	
disulfoton	Disyston	298-04-4	
methamidophos	Monitor	10265-92-6	
methidathion	Supracide	950-37-8	
methyl parathion	- -	298-00-0	
phorate	Thimet	298-02-2	
sulfotepp	Bladafume	3689-24-5	
terbufos	Counter	13071-79-9	
Carbamate insecticides:			
aldicarb	Temik	116-06-3	M
carbofuran	Furadan	1563-66-2	
methomyl	Lannate	16752-77-5	
Arsenical insecticides (especially			TM
trivalent arsenites). Examples include:	- -	7784-46-5	
sodium arsenite*	Paris Green	12002-03-8	
copper acetoarsenite*	White arsenic	1327-53-3	
arsenic trioxide*			
Methylmercury compounds* and			TM
inorganic mercurials*. Examples include:	- -	7487-94-7	
mercuric chloride*	PMA, Agrosan	62-38-4	
phenylmercuric acetate*	Panogen	151-38-2	
methoxyethyl mercury*	Ceresan M	517-16-8	
ethylmercury-p-toluene sulfonanilide*	Panogen Turf Spray	502-39-6	
methylmercury dicyandiamide*			
Rat poisons:			
sodium fluoroacetate	Compound 1080	62-74-8	M
strychnine	- -	57-24-9	TM
thallium sulfate*	Thallium	7446-18-6	
Cyanides*. Examples include:			TM
hydrogen cyanide*	Prussic acid	74-90-8	
sodium cyanide*	M-44 capsules	143-33-9	
Fumigants:			
aluminum phosphide	Phostoxin, Fumitoxin	20859-73-8	
methyl bromide	Meth-O-Gas, Brom-O-Gas	74-83-9	
sulfuryl fluoride	Vikane	2699-79-8	
Paraquat herbicide	Gramoxone	4685-14-7	M

*All or practically all uses of these pesticides have been banned by EPA or are being phased out. All other pesticides in this Table are contained in products that are almost always restricted to use by certified applicators or someone under their supervision.

From: FBI contacts for suspicious pesticide/OP nerve gas incidents: http://www.safe2use.com/ca-ipm/01-09-30.htm