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Regulatory Action Criteria for Filth and Other Extraneous Materials

III. Review of Flies and Foodborne Enteric Disease

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Forty-seven species of flies have been reliably associated with filthy conditions that might allow the spread of foodborne pathogens. These are categorized as "filth flies." Of that 47, only 21 species represent a potential threat to human health as scientifically proven causative agents of foodborne myiasis or as carriers of enteropathogenic *Escherichia coli, Salmonella, Shigella,* and other foodborne pathogens. These 21 species are categorized as "disease-causing flies" based on strict scientific criteria. The criteria are association with *E. coli, Salmonella,* AND *Shigella;* synanthropy; endophily; communicative behavior; attraction to both excrement and food products; and recognition by authorities as a potential health hazard. Within Hazard Analysis and Critical Control Point and other U.S. Food and Drug Administration regulatory frameworks, disease-causing flies are contributing factors to the spread of foodborne disease that require preventive and corrective actions as appropriate under Sanitation Standard Operating Procedures, Good Manufacturing Practices, or pest control programs.

INTRODUCTION

In the early decades of this century, flies were justly despised as purveyors of disease. With the advent of modern pest control chemicals, the direct impact of flies on the public health seemed to decline, leading to a false sense of security about the health threat that flies represent (West, 1951). Studies such as those of Watt and Lindsay (1948), Lindsay *et al.* (1953), Levine and Levine (1990), and Cohen *et al.* (1991) show how, even in modern times, inattention to sanitation can allow flies to spread foodborne diseases.

Fly contamination in food has always been a concern of the U.S. Food and Drug Administration (FDA) and its predecessors. In 1927, the federal Food, Drug, and Insecticide Administration issued a tolerance for insect filth in figs that included infestation with "vinegar flies" (Drosophilidae) (Howard, 1929). Postwar FDA publications on filth in foods include a number of articles on fly contamination in food products (Sabatino, 1954; Carson and Martinez, 1967; Gorham, 1979; Olsen *et al.*, 1993). The Agency includes flies in its manuals as significant types of filth (Gorham, 1981; Gorham, 1991a, b; Olsen, *et al.*, 1996) and has issued guidance for seafood products that defines "filth flies" to the taxonomic family level (Wisnioski, 1994). Flies are singled out in the *Code of Federal Regulations* 21 CFR 110.3(j) (Food and Drug Administration, 1997a) as a type of pest to be excluded from food-handling areas.

Traditionally, FDA has interpreted evidence of insanitation associated with flies on a case-by-case basis in relation to sections 402(a)(3) and 402(a)(4) of the Food, Drug, and Cosmetic Act. Section 402(a)(3) deems a food adulterated "if it consists in whole or in part of any filthy, putrid, or decomposed substance, or if it is otherwise unfit for food." Section 402(a)(4) deems a food adulterated "if it has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health." To date, there has been no systematic effort to refine the Agency's interpretation of fly contamination to fit modern Hazard Analysis and Critical Control Point (HACCP)-based concepts of food sanitation, especially in relation to the prevention of foodborne disease under the "rendered injurious to health" provision of section 402(a)(4) of the Food, Drug, and Cosmetic Act. Refinement is needed because, of the thousands of different types of flies, relatively few are associated with foodborne disease. Of the flies that are associated with foodborne disease, even fewer pose a realistic threat to the health of the consumer.

There are 108 families of flies containing over

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120,000 species (Borror *et al.*, 1989). Fewer than 350 fly species in 29 families are associated with the spread of disease and even fewer are associated with the spread of foodborne disease (Greenberg, 1971). Many reports of association of a fly species with foodborne pathogens are less than compelling from a public health and food sanitation standpoint. Current food safety guidance concerning fly contamination lacks the precision that is needed to differentiate the few flies that pose a true threat of the spread of disease from the many types of flies that pose a minimal health risk as potential transmitters of foodborne disease pathogens.

An example of imprecision in current guidance regarding fly filth is the blanket categorization all flies of the family Muscidae as “filth flies” (Wisnioski, 1994). Many of the Muscidae, however, are not associated with filth or insanitation (Skidmore, 1985, McAlpine, 1987). On the other hand, the Muscidae include the house fly, *Musca domestica* L., perhaps the most notorious transmitter of disease since Typhoid Mary. What is needed is refinement of the interpretation of fly contamination in foods, especially those foods that fall under the new HACCP framework.

The purpose of this review is to partition out the fly species that are reasonably likely to contribute to the spread of foodborne disease. The FDA and other food sanitation regulators can then refine the interpretation of fly filth to differentiate contamination by flies that spread disease from fly filth that represents no immediate threat to the public health. This is the third report of a series in the development of a transparent science base for a revised FDA regulatory policy in the area of filth and extraneous materials in food.

METHODOLOGY

The definitive work on the associations of flies with disease was published by Greenberg (1971, 1973). This review supplements Greenberg’s work with literature from the period 1970–1997. Information about specific foodborne pathogens was obtained from the FDA CFSAN website. Standard authoritative texts for the groups involved were used to confirm taxonomies, behavioral traits, and other biological information concerning flies (Cole, 1969; Delfinado and Hardy, 1975; Evenhuis, 1989; Ferrar, 1987; Hall, 1948; James, 1947; McAlpine, 1987; Oldroyd, 1964; Pape, 1996; Skidmore, 1985; West, 1951; Zumpt, 1965).

INTESTINAL MYIASIS

Intestinal myiasis is an invasion of the gastrointestinal tract by fly larvae. The source of intestinal myiasis is contaminated food. Scientific authorities generally agree that certain flies pose a risk to the public as agents of intestinal myiasis, especially in food contaminated by flies at the retail or consumer levels of preparation (Harwood and James, 1979; James, 1947; Godard, 1993; Greenberg, 1973; Zumpt, 1965). Haines and Rees (1989) warn that consuming fish contaminated by flies can result in intestinal myiasis. Akinbode *et al.* (1989) gave a similar warning for meat. In the literature cited below, suspect foods included fruit, undercooked or raw meat, cheese, and cooked chicken (“yakitori”).

Intestinal myiasis is a rare disease. Scott (1964) reported 28 cases of intestinal myiasis in the United States over an 11-year period (1952–1962 inclusive). About two or three cases of intestinal myiasis are reported annually in the literature (Laurence, 1986; Tachibana *et al.*, 1987; Ferreira *et al.*, 1990; Shiota *et al.*, 1990; Nakagura *et al.*, 1991; Hasegawa *et al.*, 1992; Jumaian *et al.*, 1995; Lee *et al.*, 1995; Chung *et al.*, 1996). Recent morbidity statistics for calendar year 1984 report nine cases of intestinal myiasis over a year’s time (Madison *et al.*, 1985) and there are undoubtedly many unreported cases (Laurence, 1986).

All segments of the population are at risk of myiasis from contaminated food (Godard, 1993; Jumaian *et al.*, 1995; North, *et al.*, 1987). Normally, the seriousness of intestinal myiasis is limited (transitory minor disability and annoying complaints) (James, 1947; Zumpt, 1965), but it can become moderate (transient but significant disability) when the fly larvae embed themselves in the appendix or otherwise damage the tissue of the intestine (Harwood and James, 1979; Kenney *et al.*, 1976). Although flies cannot grow to maturity and reproduce in the gastrointestinal tract, there is evidence that larval development takes place there (Banks, 1912; Jettmar, 1940; James, 1947; Busvine, 1966; Barkin *et al.*, 1983).

The literature on intestinal myiasis has been extensively reviewed (James, 1947; Baumgartner, 1988; Zumpt 1965). Data from these reviews can be combined with data from more recent reports of intestinal myiasis (*e.g.*, Furman *et al.*, 1959; Kilpatrick and Schoof, 1959; Scott and Littig, 1964) to derive a list of flies that are reliably reported to cause intestinal myiasis in humans. The resulting list is summarized in Table 1.

Reports that are based solely on finding larvae in stool samples are not conclusive proof of foodborne myiasis. Several explanations for this phenomenon are possible. A report of intestinal myiasis must contain additional observations that verify the foodborne origin of the fly larvae in order to be credible (Busvine, 1966). Additional observations may include surgical recovery of fly larvae from a victim’s intestine, recovery of fly larvae from food consumed by a victim, recovery of fly larvae from vomit, or recovery of fly larvae from a victim’s stool under clinical conditions where the possibility of cross-contamination was controlled. Table 1 is based on reports of intestinal myiasis that meet this additional observation criterion.

TABLE 1
Examples of Fly Species Known to Cause Intestinal Myiasis in Humans

Fly species	Family	References
Megaselia insulana Brues	Phoridae	Ferriera *et al.*, 1990
Piophila casei (L.)	Piophilidae	Zumpt, 1965
Hermetia illuscens (L.)	Stratiomyidae	Nagakura *et al.*, 1991; Lee *et al.*, 1995
Erstalis tenax (L.)	Syrphidae	James, 1947
Fannia spp.	Muscidae	James, 1947
Muscina stabulans (Fallén)	Muscidae	Laurence, 1986; North *et al.*, 1987
Stomoxys calcitrans (L.)	Muscidae	Ferriera *et al.*, 1990
Calliphora vicina (Robineau-Desvoidy)	Calliphoridae	Zumpt, 1965
Phormia regina (Meigen)	Calliphoridae	Kenney *et al.*, 1976
Phaenicia cuprina Wiedemann	Calliphoridae	Jumaian *et al.*, 1995
Sarcophaga (including Jantia) spp.	Sarcophagidae	Kenney *et al.*, 1976; Tachibana *et al.*, 1987; Shiota *et al.*, 1990

THE FLY AS A CARRIER OF DISEASE

The evidence relating to the transmission of foodborne pathogens by flies consists of case control epidemiological studies, fly population suppression studies and field studies of transmission by flies that are fed from infected reservoirs. As passive vectors, certain flies are capable of contaminating food with *Shigella*, *Salmonella*, disease-causing *Escherichia coli*, *Campylobacter jejuni*, *Vibrio cholera*, and other foodborne pathogens (Greenberg, 1973; Levine and Levine, 1991). In this situation, flies amplify the risk of foodborne disease by transporting pathogens from places where the pathogens pose no hazard to places where they do (Gorham, 1989). All segments of a population are at risk of gastroenteritis from food contaminated with the pathogens noted above. The seriousness of gastroenteritis is limited (transitory minor disability; annoying complaints) unless a patient's health is otherwise compromised (Bean *et al.*, 1990). Infant morbidity and mortality from gastroenteritis is generally higher than that of other groups, but the literature contains no reports that link a fly-related epidemic with elevated infant mortality. The sources of epidemics of foodborne illnesses are unknown in approximately one-fourth of the incidents reported each year (Bean *et al.*, 1990) and flies may contribute to some of these (West, 1951).

Flies are holometabolous insects, with a life cycle that includes egg, larva, pupa, and adult. The larvae of muscoid flies, *e.g.*, families Muscidae (house flies), Calliphoridae (blow flies), and Sarcophagidae (flesh flies), are headless, legless vermiform maggots. Adults are bristly robust flies, generally 5 mm or more in body length. A typical life cycle (egg to adult) ranges from 1 week to 2 months under normal environmental conditions. Females may lay up to 700 eggs in a lifetime and there may be 6 to 10 or more generations per year (James, 1947). The typical muscoid adult has been demonstrated to transmit pathogens on the sponging mouthparts, through vomitus, on body and leg hairs, on the sticky pads of the feet, and through the intestinal tract (Radvan, 1960). It has been demonstrated that the microorganisms on a fly's body are disseminated by direct contact (Sulaiman *et al.*, 1988; Sramova *et al.*, 1992; Richards *et al.*, 1961; Paraluppi *et al.*, 1996; Greenberg, 1964; Echeverria *et al.*, 1983; De Capito, 1963; Bolanos, 1959; Akinbode *et al.*, 1989; Khin *et al.*, 1989), in fly feces (Greenberg *et al.*, 1970), and through the air for short distances from insect-electrocuting traps (Pickens, 1989; Broce, 1993; Tesch and Goodman, 1995; Ananth *et al.*, 1992).

EFFECTS ON MORBIDITY OF CONTROLLING FLY POPULATIONS

Natural populations of flies are known to harbor *Campylobacter jejuni*, *Entamoeba histolytica*, disease-causing *E. coli*, *Salmonella* spp., *Shigella* spp., *Staphylococcus aureus*, and *Vibrio cholera* (Hormaeche *et al.*, 1950; Coleman and Maier, 1956; Bolanos, 1959; Richards *et al.*, 1961; DeCapito, 1963; Sakdisiwasdi *et al.*, 1972; Biwald *et al.*, 1978; Gorham, 1991; Olsen *et al.*, 1993; Iwasa *et al.*, 1998; Sanada *et al.*, 1998). An example of the extent to which flies may harbor foodborne pathogens is the house fly, *Musca domestica*. Table 2 lists examples of foodborne pathogens harbored by *M. domestica*. Other examples of isolations of

TABLE 2
Examples of Foodborne Pathogens Isolated from Natural Populations of House Flies, *Musca domestica* L.

Pathogen	Reference
Campylobacter jejuni	Roosef and Kapperud, 1983
Entamoeba histolytica	Buxton, 1920
Escherichia coli (pathogenic)	Echeverria *et al.*, 1983; Sanada *et al.*, 1998
Salmonella typhimurium	Floyd and Cook, 1953
Shigella (five species)	Levine and Levine, 1990
Vibrio cholera 0139	Sengupta *et al.*, 1995

foodborne pathogens from natural fly populations implicate blow flies (*Chrysomya* and *Phaenicia*) as harboring *Salmonella, E. coli,* and *Shigella* (Sulaiman *et al.*, 1988; Paraluppi *et al.*, 1996). In addition, researchers have discovered natural harboring of infective parasites (*Giardia, Taenia, Ascaris,* and *Trichiurus*) on Oriental latrine flies, *Chrysomya megacephala* (F.); house flies, *Musca domestica* L.; and flesh flies, *Sarcophaga* sp. (Harris and Down, 1946; Lawson and Gemmell, 1985; Sulaiman *et al.*, 1988, 1989; Jackson and Mahady, 1989; Mariluis *et al.*, 1989; Monzon *et al.*, 1991).

Epidemiological studies have been conducted to determine the effect that reducing fly populations has on the morbidity of foodborne enteric disease. To date, studies have focused on shigellosis with secondary efforts to assess the impact of fly control on salmonellosis. Levine and Levine (1990) thoroughly reviewed these studies, which are summarized below. The available epidemiological studies indicate that certain flies are a significant factor in the spread of foodborne diseases and that control of fly populations is an important factor in the prevention of enteric illnesses.

Kuhn and Anderson (1944) reported an outbreak of dysentery in a military camp that coincided with sudden population explosion of flies.

Compelling field epidemiology studies were conducted by Watt and Lindsay (1948) and Lindsay *et al.* (1953) in south Texas and south Georgia that found statistically significant positive correlations between fly populations and the incidence of shigellosis and salmonellosis. The studies were conducted in areas of high morbidity and moderate morbidity, respectively. The studies are significant in that fly populations were quantitatively documented with Scudder fly grids and the intervention that was taken during the studies was to suppress fly populations through pesticide applications. A study conducted in Egypt (Weir *et al.*, 1952) also indicated correlation between shigellosis and suppression of fly populations.

Cohen *et al.* (1991) found a statistically significant positive correlation between fly populations and shigellosis in a military camp in the Persian Gulf. Suppression of fly populations in the camp resulted in an 85% decrease in shigellosis and a 42% decrease in the incidence of diarrheal diseases. These data were confirmed by clinical tests that demonstrated correlative changes in antibodies to *Shigella* and enterotoxigenic *E. coli* (ETEC) in equivalent groups of soldiers. The study took place in 1988 and was replicated in 1989 with similar results.

Esrey (1991) reported fly suppression studies that achieved up to 40% reductions in the frequency of diarrheal disease among children. The report concluded that even though fly suppression was effective in reducing morbidity and mortality from infantile diarrhea, it was not a sustainable form of intervention from an economic standpoint. This conclusion is disputed by other authorities (Chavasse *et al.*, 1994).

Studies conducted in hospitals provide insight on the ability of flies, especially the house fly, to transmit foodborne pathogens such as *Salmonella, Shigella,* and *V. cholera* (*e.g.*, Chow, 1940; Fotedar *et al.*, 1992; Sramova *et al.*, 1992). By isolating the impact of flies from other epidemiological factors, hospital studies demonstrate that flies are, indeed, capable of spreading foodborne diseases. These studies demonstrate a capacity to transmit foodborne pathogens that qualifies flies as a potential source of cross-contamination in any environment where sanitation lapses, giving the flies access to exposed food or food-contact surfaces (Levine and Levine, 1991).

Other studies have noted correlations between the suppression of flies and reduction of enteric disease. In a study comparing levels of bacteria in flies in Peking, China, Yao *et al.* noted an apparent positive correlation between numbers of bacteria per fly and incidence of enteric infections. Peffly (1953) recounts an observation of reduced infant mortality that he attributes to a fly suppression program in a village in Egypt. These studies, however, lack a statistical treatment of the data. All of the above studies include observations of resurgence of enteric disease following the termination of fly suppression programs.

RISK ASSESSMENT STUDIES

Epidemiological studies normally find that factors such as water quality, sanitation, and hygiene are the primary risk factors in the spread of many enteric diseases (*e.g.*, Yao *et al.*, 1929; Black *et al.*, 1978; Zeitlin *et al.*, 1995). Relatively little has been done in the area of risk assessment involving flies. Some risk assessment studies that do consider flies simply assess the statistical risk associated with the presence of flies (*e.g.*, Zeitlin *et al.*, 1995). Two recent case control studies, however, explore in more detail the role of flies as passive vectors of pathogens in multivehicular situations.

The relative risk associated with fly transmission of foodborne pathogens was considered in a recent case–control study of diarrhea in children in Malaysia. Although untreated drinking water was the primary risk factor, exclusion of flies from food was assigned an associated minor risk factor nearly equivalent to that of hand-washing on the part of the children's caregivers (Knight *et al.*, 1992). A similar recent study of intrafamilial transmission of cholera in India found that cholera pathogens were recovered from the washings of the hands of contacts of index cases (2 of 54 samples) nearly as often as the pathogen was recovered from groups of flies captured in the homes of index cases (1 of 26 samples). The results from control households found no cholera in 21 hand-washing samples and 14 fly samples (Sengupta *et al.*, 1995). Both studies involved house flies and blow flies. While the statistical significance of these results is low the studies suggest that, in efforts to prevent these diseases, failures to control flies carry an odds ratio that is comparable to the risk of failures to wash hands.

TRANSMISSION OF PATHOGENS BY FLIES

The epidemiology studies indicate that certain flies are capable of transmitting foodborne enteric diseases on a large, occasionally epidemic, scale. Gorham (1989) notes the relative lack of proven individual cases of human illness caused by a pathogen carried to a person's food by flies. Gorham and others also note that the habits of flies, especially their indiscriminate travel between filth and food, are so well known that there is no question about the wisdom of excluding disease-carrying flies from food and food-contact surfaces (Bohart and Gressit, 1951; Chavasse *et al.*, 1994).

Pathogen-laden flies have been shown to travel between pathogen reservoirs and exposed food (Wilton, 1961; Mayr, 1983; Daniel *et al.*, 1989; Khin *et al.*, 1989; Khalil *et al.*, 1994). In a pair of studies in Mexico, Greenberg demonstrated that house flies and blow flies transported *Salmonella* from a slaughterhouse to a nearby market and to nearby residential areas (Greenberg, *et al.*, 1963; Greenberg and Bornstein, 1964). An earlier study found house flies transporting *Salmonella enteriditis* from a sewage pool to a kitchen three miles distant (Pepper, 1944).

Greenberg (1964) conducted a study in which he fed *Salmonella typhimurium* to house flies and then allowed the house flies to feed on exposed food. He then fed the fly-contaminated food to 10 volunteers. Stool samples from 6 of the 10 volunteers subsequently tested positive for *S. typhimurium* where none had tested positive prior to the feeding. None of the 10 volunteers showed clinical symptoms of salmonellosis because Greenberg avoided administering the massive dose of *S. typhimurium* to the experimental flies that would be necessary to evoke symptoms in the test volunteers. While the relative morbidity risk from fly-transmitted pathogens in food is normally small, the above studies demonstrate that this risk is not negligible or trivial.

The evidence concerning the links between flies and the spread of foodborne diseases is not easily extracted and organized due to the sheer volume of the material. The encyclopedic work of Greenberg (1971) contains a bibliography of 84 pages of journal citations for articles that establish bionomic and epidemiologic associations of flies with various diseases. Greenberg's data encompass 346 fly species in 29 families. Half of the database is devoted to veterinary medicine and diseases of animals. The portion of Greenberg's data concerned with human diseases is partitioned into 19 categories, three of which (cholera, enteric infections, and helminth diseases) are also areas of concern for the FDA regulatory mission. Greenberg's enteric infections category includes the microorganisms that are most often encountered as foodborne pathogens (*E. coli*, *Salmonella*, and *Shigella*), while cholera and helminths are only occasionally found in food products regulated by FDA. Of the three categories that concern FDA, the pathogens in the enteric infections category form the broadest basis for refining the interpretation of fly contamination of food.

Once the information relating to foodborne pathogens is examined in detail, Greenberg's review leaves no doubt that behavior and population dynamics can make some fly species more dangerous than others as potential transmitters of disease. In addition, some segments of the human population are more vulnerable to foodborne infections that are spread by flies because of their underlying host factors (*e.g.*, underlying medical conditions). To determine which species realistically represent a serious threat of transmission of foodborne diseases, it is necessary to consider both bionomics and epidemiology.

INTERPRETING THE BIONOMIC DATA

Bionomics can address whether a particular species represents a credible threat of transmitting foodborne disease by providing answers to the following questions: (1) Does the life history of the species involve visits by the adult fly to potential reservoirs of pathogens and (2) is the species synanthropic or otherwise likely to occur in habitats where it comes in contact with food and food-contact surfaces?

The data compiled by Greenberg addresses these questions of bionomics. Table 3 lists the flies that are known to visit likely reservoirs (*i.e.*, excrement and sewage) of the foodborne pathogens included in Greenberg's enteric infections category. The list was compiled from various sources (James, 1947; Wilton, 1961; Greenberg, 1971, 1973; Mayr, 1983). A fly species was included in Table 3 only after confirmation by reports in the scientific literature of association with *E. coli*, an indicator organism associated with sewage and excrement. Table 3 also lists the number of literature references given by Greenberg in support of association of each fly with *E. coli*.

Seventeen of the species in Table 3 are species that Greenberg's review also associates with *Salmonella* and *Shigella*. The 17 species are recognized as medically important vectors of disease (Pittaway, 1991). A search of the literature from 1970 to present found no additional species that have been associated with all three pathogens. Fly species associated with multiple types of foodborne pathogens are, by definition, disease-causing flies. The 17 species, along with the num-

TABLE 3
Filth Flies Associated with *E. coli* (Reference Citations from Greenberg, 1971)

Fly Species	Family	No. reference citations
Physiphora demandata (F.)	Otitidae	1
Sepsis punctum (F.)	Sepsidae	1
Piophila casei (L.)	Piophilidae	3
Piophila pectiniventris Duda	Piophilidae	1
Copromyza atra (Meigen)	Sphaeroceridae	1
Leptocera ferruginata (Stenhammar)	Sphaeroceridae	1
Limosina punctipennis (Wiedemann)	Sphaeroceridae	1
Scathophaga stercoria (L.)	Scathophagidae	1
Hylemya cinerella (Fallén)	Anthomyiidae	1
Anthomyia pluvialus (L.)	Anthomyiidae	1
Mydaea urbana (Meigen)	Muscidae	1
Fannia canicularis (L.)	Muscidae	5[a]
Fannia incursurata (Zetterstedt)	Muscidae	1
Fannia scalaris (F.)	Muscidae	3
Fannia leucosticta (Meigen)	Muscidae	1
Hydrotaea dentipes (F.)	Muscidae	1
Hydrotaea irritans (Fallén)	Muscidae	1
Hydrotaea occulata (Meigen)	Muscidae	1
Ophyra leucostoma (Wiedemann)	Muscidae	3
Lasiops simplex (Wiedemann)	Muscidae	1
Phaonia incana (Wiedemann)	Muscidae	1
Phaonia querceti (Bouche)	Muscidae	1
Muscina stabulans (Fallén)	Muscidae	5[a]
Synthesiomyza nudiseta (Wulp)	Muscidae	1
Orthellia caerula Wiedemann	Muscidae	1
Musca domestica L.	Muscidae	38[a]
Musca larvipara Porchinskii	Muscidae	1
Haemotobia irritans (L.)	Muscidae	1
Stomoxys calcitrans (L.)	Muscidae	2[a]
Cochliomyia macellaria (F.)	Calliphoridae	1[a]
Chrysomya megacephala (F.)	Calliphoridae	2[a]
Chrysomya pinguis (Walker)	Calliphoridae	1
Chrysomya putoria (Wiedemann)	Calliphoridae	1[a]
Phormia regina (Meigen)	Calliphoridae	2[a]
Protophormia terraenovae (R.-D.)	Calliphoridae	5[a]
Lucilia caesar (L.)	Calliphoridae	4[a]
Phaenicia cuprina Wiedemann	Calliphoridae	1
Phaenicia sericata (Meigen)	Calliphoridae	7[a]
Aldrichina grahami (Aldrich)	Calliphoridae	1
Calliphora vicina (R.-D.)	Calliphoridae	10[a]
Calliphora vomitoria (L.)	Calliphoridae	6[a]
Cynomyopsis cadaverina (R.-D.)	Calliphoridae	1[a]
Sarcophaga argyrostoma (R.-D.)	Sarcophagidae	1
Sarcophaga carneria (L.)	Sarcophagidae	5[a]
Sarcophaga haemorrhoidalis (Fallén)	Sarcophagidae	2[a]
Sarcophaga hirtipes Wiedemann	Sarcophagidae	1
Sarcophaga melanura Meigen	Sarcophagidae	1

[a] Also associated with *Salmonella* and *Shigella*.

ber of references from Greenberg (1971), are listed in Table 4.

There are additional criteria for categorizing a disease-causing filth fly as a possible threat to human health. In order to transmit foodborne pathogens to humans, a fly must be synanthropic (living around human settlements). A fly that lives only in remote areas away from people is not a threat to human health. The 17 flies that are listed in Table 4 as associated with the three common foodborne pathogens are all definitely categorized as synanthropic (James, 1947; Bohart and Gressitt, 1951; Greenberg, 1971, 1973).

Another factor to consider is whether a species exhibits "communicative" behavior. Greenberg (1971) defines communicative as "oscillating between the contaminated environment and man's surroundings." A disease-causing filth fly that is not attracted to human food as well as to potential reservoirs of pathogens is unlikely to represent much of a threat in terms of

TABLE 4

Number of Literature References (from Greenberg, 1971) for Associations of Flies with Foodborne Pathogens

Fly species	No. References for Association with		
	E. coli	*Salmonella*	*Shigella*
Fannia canicularis	5	1	2
Fannia scalaris	3	1	2
Muscina stabulans	5	1	3
Musca domestica	38	25	30
Cochliomya macellaria	1	3	1
Stomoxys calcitrans	2	2	1
Chrysomya megacephala	2	2	2
Chrysomya putoria	1	1	1
Phormia regina	2	4	2
Protophormia terraenovae	5	2	1
Lucilia caesar	4	5	4
Phaenicia sericata	7	8	3
Calliphora vicina	10	5	3
Calliphora vomitoria	6	3	3
Cynomyopsis cadaverina	1	3	1
Sarcophaga carneria	5	3	2
Sarcophaga haemorrhoidalis	2	1	2

transmission of foodborne pathogens. Fourteen of the 17 flies listed in Table 4 are classified by Greenberg as communicative. The exceptions are *Phormia regina*, *Protophormia terraenovae*, and *Lucilia caesar*. The 14 remaining flies are all synanthropic, communicative, and known to be attracted to human food, excrement, and garbage (Hall, 1948; Bohart and Gressitt, 1951; Greenberg, 1973; Skidmore, 1985; Daniel *et al.*, 1989). Most of these flies are also attracted to seafood and fisheries products (Bohart and Gressitt, 1951; Okaeme, 1986; Walker and Donegan, 1988; Haines and Rees, 1989; Olsen and Sidebottom, 1990; Esser, 1990, 1991; Olsen *et al.*, 1992; d'Almeida and de Mello, 1996; d'Almeida and Salviano, 1996). Many have been isolated from foods examined by FDA scientists (Hamm and Olsen, 1979; Olsen, 1988; Olsen *et al.*, 1993; Olsen, 1996).

INTERPRETING THE EPIDEMIOLOGICAL DATA

The epidemiological questions that must be asked are (1) does the species have a compelling history of transmission of foodborne pathogens or is the species itself an agent of disease (myiasis) associated with consuming contaminated food, (2) is there reason to conclude that suppression of the species can affect human morbidity and mortality from foodborne diseases, and (3) is there opportunity for the fly species to contaminate the kinds of food that can support rapid growth of foodborne pathogens or other undesirable microorganisms?

The effectiveness of suppression of flies to prevent enteric disease is difficult to evaluate because of the epidemiological complexity and multivehicular spread of foodborne diseases generally. Greenberg (1973) reviews a total of 38 journal articles reporting reductions in enteric disease correlated to fly suppression, but the authors of these articles rarely reported identifications of the fly species or supportive statistical analysis. Three flies, however, were involved in recent studies where the suppression of these specific flies is statistically correlated to significant reductions in morbidity from enteric infections. These flies are *Musca domestica*, *Chrysomya* sp., and *Phaenicia sericata* (Levine and Levine, 1990; Cohen, 1991).

Other key epidemiological considerations are the mobility of flies and the sizes of fly populations. Because of their mobility, disease-causing flies are capable of delivering viable pathogens from remote reservoirs to food and food-contact surfaces (Greenberg, 1964; Greenberg *et al.*, 1963; Greenberg and Bornstein, 1964; Wilton, 1961). This is an important HACCP consideration because delivery of viable pathogens to food or food-contact surfaces at a point subsequent to the application of a biocidal processing step may render the biocidal step ineffective. Another mobility consideration is the spread of exotic fly species that are more efficient carriers of pathogens. For example, the blow fly *Chrysomya megacephala* (F.) (Calliphoridae) has invaded North and South America within the past two decades (Olsen and Sidebottom, 1990; Hogue, 1993). This invader displaces native flies and represents a much greater health hazard in terms of capacity to deliver pathogens to foods (Greenberg, 1988; Olsen, *et al.*, 1993).

The question of whether an organism as small as a fly can deliver an infective dose of a pathogen to an exposed food has not been scientifically explored. The actual number of cells that a single fly can carry and transfer to a food may not be a critical factor. The flies that are associated with foodborne pathogens often exhibit clustering and swarming behavior that ensures that large numbers of them will visit a particular site on an exposed food (Kano, 1958; Olsen *et al.*, 1993; Godoy *et al.*, 1996) with a cumulative effect that overpowers the carrying capacity of a single fly. Numbers of flies may be the most important factor in this respect.

Fly populations can explode with tremendous numbers in a short period of time (Norris, 1965). A recent forensic study of fly migration in Louisiana reported adult emergences of *P. sericata* and other blow flies from the ground at the rate of 2370 per m^2 in the vicinity of a simulated cadaver (Tessmer and Meek, 1996). Such impressive numbers help put a perspective on the risk of allowing the above pests uncontrolled opportunities to repeatedly visit exposed food.

High densities of flies increase the load of pathogens that are delivered to a food or food-contact surface. The clustering and aggregation behaviors that are characteristic of some disease-causing flies (*e.g.*, Olsen and Sidebottom, 1990; Godoy *et al.*, 1996) concentrate the delivery of pathogens to sites where infective doses may quickly accumulate. The situation is analogous to that of contact by unwashed hands or utensils, where a single touch from an unwashed finger does not necessarily deliver an infective dose of pathogens to a food but multiple contacts, which are virtually assured, increase the odds of cross-contamination with each successive exposure of the food product to a potential source of cross-contamination (Lindsay and Scudder, 1956).

From an epidemiological standpoint the prevention of intestinal myiasis is more straightforward. Intestinal myiasis is prevented by suppression of the fly species that are the causative agents (James, 1947; Zumpt, 1965). Other preventive measures may include visual examination of food before consumption, excluding myiasis-causing species from contact with food, or thorough cooking of food to kill myiasis-causing maggots.

REVISITING THE CONCEPT OF A "FILTH FLY"

The taxonomic families that are included in the FDA category of "filth fly" (Wisnioski, 1994) were chosen on the basis that each family contains members that breed in excrement or have otherwise "filthy" habits or behaviors (*e.g.*, visiting garbage or feces, breeding in cadavers, *etc.*). As noted in the introduction, not all members of a particular family share the same habits or behaviors. Breeding in excrement, however, is one criterion for defining what constitutes a filth fly. Coliforms, especially *E. coli*, are considered a reliable indicator of fecal contamination. The data presented above indicate that at least 47 fly species are filth flies based on their proven association with *E. coli* and known attraction to excrement or other filth. Table 3, containing these 47 species, is a core list of known filth fly species.

The use of Table 3 as a core list of filth flies is consistent with conclusions drawn by modern medical entomologists. Godard (1993) defines filth flies as members of the families Muscidae, Calliphoridae, and Sarcophagidae, a position he shares with other medical entomologists (*cf.* Harwood and James, 1979). The vast majority of the flies in Table 3 belong to these three families.

Association with filthy habitats, however, does not necessarily mean that a fly is actually capable of transmitting pathogens to humans. Very few of the "filth flies" listed in Table 3 can, within reason, be so strongly associated with the transmission of disease as to pose a serious threat to the public health. Three genera of flies have been statistically proven through fly suppression and other epidemiological studies to be capable of transmitting foodborne pathogens to humans. These flies share certain attributes that account for their strong association with the transmission of foodborne disease. These shared attributes (from Greenberg, 1971) are: (1) wild (natural) populations associated with *E. coli*, *Salmonella*, AND *Shigella*, (2) synanthropy (preferring human habitats), (3) endophily (entering buildings), (4) communicative behavior, (5) attraction to both excrement and food products, and (6) recognition by medical entomology authorities as potential threats to public health from the transmission of enteric pathogens.

Flies that share in common the above attributes are a more serious public health concern than the majority of the filth flies listed in Table 3. The flies from Table 3 that meet the above criteria all belong to the genera *Musca*, *Chrysomya*, *Phaenicia*, *Calliphora*, *Cochliomyia*, *Cynomyopsis*, and *Sarcophaga* (including *Jantia*).

As a reasonable precaution, the flies listed above should be considered a potential health hazard even though epidemiological suppression studies have yet to be conducted for all. This conclusion is based on the bionomic attributes shared with the three pathogen-carrying flies for which suppression studies have established a positive correlation between flies and enteric disease.

In addition to the known carriers of foodborne pathogens, it is necessary to consider the myiasis-producing flies that are direct agents of foodborne disease. Table 5 extracts the fly species of the above genera from Table 4 that are known carriers of multiple types of pathogens and combines these species with seven additional species (Table 1) that are known agents of intestinal myiasis but not always strongly associated with the transmission of pathogens. The combined list in Table 5 represents the fly species that are convincingly documented in the scientific literature as having the six attributes (described above) for defining a fly species as a reasonably likely agent of foodborne disease in human beings.

FILTH FLIES IN THE HACCP ENVIRONMENT

The presence of disease-causing flies in a food-handling establishment constitutes a potentially hazardous HACCP situation (Gorham, 1989). The threat posed is the threat of a contributing factor that could cross-contaminate food with in-plant pathogens, contaminate food with pathogens or myiasis-causing larvae, or circumvent an otherwise effective biocidal critical control point.

Current HACCP regulations found in 21 CFR 123.11(b)(8) (Food and Drug Administration, 1997a) and related Good Manufacturing Practice (GMP) regulations in 21 CFR 110.20(a)(1), 21 CFR 110.35(c), and 21 CFR 110.37(f) require the exclusion of pests from areas where food is manufactured, packed, or held

TABLE 5
Examples of Flies That Pose a Potential Health Hazard from Foodborne Disease

Species	Family	Disease potential
Hermetia illuscens (L.)	Stratiomyidae	Intestinal myiasis
Megaselia insulana Brues	Phoridae	Intestinal myiasis
Eristalis tenax (L.)	Syrphidae	Intestinal myiasis
Piophila casei (L.)	Piophilidae	Intestinal myiasis
Fannia canicularis (L.)	Muscidae	Intestinal myiasis, vector of enteric pathogens
Fannia scalaris (F.)	Muscidae	Intestinal myiasis, vector of enteric pathogens
Musca domestica L.	Muscidae	Vector of enteric pathogens
Muscina stabulans (Fallén)	Muscidae	Intestinal myiasis
Stomoxys calcitrans (L.)	Muscidae	Intestinal myiasis, vector of enteric pathogens
Calliphora vicina (Robineau-Desvoidy)	Calliphoridae	Intestinal myiasis, vector of enteric pathogens
Calliphora vomitoria (L.)	Calliphoridae	Vector of enteric pathogens
Chrysomya megacephala (F.)	Calliphoridae	Vector of enteric pathogens
Chrysomya putoria (Wiedemann)	Calliphoridae	Vector of enteric pathogens
Cynomyopsis cadaverina (R.-D.)	Calliphoridae	Vector of enteric pathogens
Cochliomyia macellaria (F.)	Calliphoridae	Vector of enteric pathogens
Phaenicia cuprina Wiedemann	Calliphoridae	Intestinal myiasis
Phaenicia sericata (Meigen)	Calliphoridae	Vector of enteric pathogens
Phormia regina (Meigen)	Calliphoridae	Intestinal myiasis, vector of enteric pathogens
Sarcophaga (=Jantia) crassipalpis (Macquart)	Sarcophagidae	Intestinal myiasis
Sarcophaga carneria (L.)	Sarcophagidae	Vector of enteric pathogens
Sarcophaga haemorrhoidalis (Fallén)	Sarcophagidae	Intestinal myiasis, vector of enteric pathogens

(Food and Drug Administration, 1997b). Flies are specifically named in 21 CFR 110.3(j) as an example of the kind of pest that shall be excluded from food-processing and food-storage establishments (Food and Drug Administration, 1997b). The control of flies and other pests would not normally be accomplished through the critical control points (CCPs) of a HACCP plan, but rather through prerequisite Sanitation Standard Operating Procedures. The proper venue for controlling the transmitters or vectors of foodborne pathogens is an effective sanitation and pest-exclusion program. Such a program controls and eliminates pests from food-processing areas is a mandatory prerequisite to a HACCP plan (Food and Drug Administration, 1997b).

A balanced approach to excluding flies from food-handling and storage areas depends on differentiating between the relatively few fly species that are reasonably likely to contribute to human morbidity and mortality from foodborne disease and the many kinds of flies whose association with the spread of foodborne disease is less compelling. Failure to exclude a disease-transmitting or disease-causing species (*e.g.*, a species listed in Table 5) from a food-processing facility is grounds for evaluating whether an otherwise effective microbiological CCP is likely to have been circumvented or otherwise compromised by insect pests (Gorham, 1989; Olsen *et al.*, 1993). The HACCP sanitarian must address the epidemiological question of whether there is opportunity for the fly species to contaminate the kinds of food that can support the rapid growth of the foodborne pathogens or other undesirable microorganisms which the fly species is known to transmit. The answer to this question depends not only on the bionomics of the fly but also on the food-handling process, the intended use of the product, and other standardized HACCP considerations for the control of microbiological food safety hazards and contributing factors such as flies.

This requires that sanitation control professionals know how to recognize the adult and larval stages of the few fly species that are a potential health threat and be able to accurately connect the fly species with a reasonably likely hazard so that, if necessary, appropriate preventive and corrective actions can be taken. The level of concern appropriate for a particular fly species depends, in part, on the degree to which the species is associated with the spread of foodborne disease. It must be emphasized that there is no known health hazard associated with the vast majority of fly species.

CONCLUSIONS: REGULATORY SIGNIFICANCE OF FLIES

Flies as well as other notorious carriers of foodborne pathogens (*e.g.*, cockroaches, mice, rats, and birds) merit serious consideration as contributing risk factors in the HACCP environment of modern food sanitation (Minette, 1984; Gorham, 1989; Olsen, *et al.*, 1996). Because flies harbor pathogens in natural populations, it is necessary to prevent these flies from gaining access to human food and food-contact surfaces (Levine and Levine, 1991). A sanitary environment (including exclusion of flies) and safe water are among the highest priorities for reducing morbidity from foodborne disease (Khalil *et al.*, 1994). The summary below describes, in general terms, the potential hazards from "disease-causing flies" that should be considered in making regulatory decisions.

Flies of any species should be excluded from food-handling areas in accordance with current HACCP and GMP regulations regarding exclusion of pests (Food and Drug Administration, 1997a, b). The currently available FDA regulatory guidance for fly filth is limited in amount and scope. These criteria are published as guidelines for "filth insects" in imported seafood (Wisnioski, 1994) and as FDA Compliance Policy Guides for fly filth in various products including milk used in the manufacture of cheese products, cherries, citrus fruit juices, olives, raisins, mushrooms, spinach, tomato products, *etc.* (Michels and Schroff, 1996). As previously noted, the established criteria lack the levels of precision needed by modern regulators, sanitarians, and HACCP planners to accurately evaluate the true potential health risks from fly contamination. This lack of precision can result in grouping unavoidable and harmless types of fly contamination with contamination from disease-causing flies and vice versa.

The six bionomic and behavioral attributes that define whether a fly species poses a bona fide risk to human health from foodborne disease are summarized in this review. These attributes provide a more precise set of objective, scientific criteria for interpreting fly contamination of food products in both HACCP and non-HACCP food-processing environments. The attributes can be applied to fly contamination covered under existing regulatory guidelines so the guidelines can be uniformly applied and to fly contamination found in situations where no regulatory guidance exists.

Table 3 contains verified examples of flies that are associated with pathogens and insanitary conditions. The flies in Table 3 are classified as filth flies (*cf.* James and Harwood, 1979; Godard, 1993) that are objectionable and avoidable types of filth under the provisions of sections 402(a)(3) and 402(a)(4) of the Food, Drug, and Cosmetic Act.

Table 5 contains verified examples of the flies that pose potential health hazards because they either cause intestinal myiasis and/or possess the six attributes that make a species a threat to human health as a carrier of foodborne disease. In addition to being objectionable and avoidable filth, the flies in Table 5 may represent insanitary conditions "whereby a product may have been rendered injurious to health," either as causes of myiasis or as contributing factors to the spread of foodborne pathogens.

In essence, food-contaminating flies can be characterized in different ways depending on whether biocidal processing steps, intended use of the product, and other factors neutralize or eliminate the potential health hazards involved. If the potential hazards are not effectively neutralized or eliminated, the flies in Table 5 require heightened regulatory concern under the "injurious to health" provision of section 402(a)(4). Tables 1 through 5 serve as a basis for effective public health planning in the areas of pest control in and around areas where human food is manufactured, packed, or stored. The information in these tables also provides a list of potential hazards from flies to be considered in planning pest-control programs and corrective actions to prevent or correct potential microbial contamination or cross-contamination from flies.

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