Risk Assessment

In this guide

In the UK the frequency of occurrence of foodborne botulism is very low (very rare but cannot be excluded). However, the severity of botulism is classified as high (severe illness: causing life threatening or substantial sequelae or long-term illness). High severity demands that risk assessments for foodborne botulism should be regularly updated to keep in step with the changing practice of food production and with improved understanding of the biology of *C. botulinum* and other neurotoxigenic clostridia.

In 2005 EFSA published the opinion of their BIOHAZ panel with regard to *Clostridium* spp. in foodstuffs[254]. In addition several process risk assessments relating to *C. botulinum* for specific food products or processes have been published in the scientific literature; examples include packaged smoked fish in New Zealand[255], canned foie gras in France[256] and chilled dairy-based foods in the UK[257]. Many national authorities, including the UK NHS[258], maintain up to date fact sheets promoting awareness of botulism risks.

Other forms of botulism including infant botulism, adult infectious botulism, wound botulism and inhalation botulism involve different risk pathways and each requires risk assessment that is distinct from that for foodborne botulism.

6.1 Hazard identification

Spores of *C. botulinum* occur widely in the environment and cannot reliably be excluded from unprocessed food materials. Vegetative growth of *C. botulinum*, or other neurotoxigenic clostridia, may produce potent botulinum neurotoxins so that, in the absence of measures which prevent spore germination and population growth in food prior to consumption, the organism and the botulinum neurotoxin are identified as hazards.

Chilled foods establish a limited period of storage at low temperatures (not exceeding 8°C) that with other controlling factors prevents growth and/or toxin formation by non-proteolytic *C. botulinum*. Chilled storage alone is sufficient to prevent growth and toxin formation by proteolytic *C. botulinum*. Chemical conditions within the food often contribute additional control. Failures of the temperature or chemical controls are identified with hazards from *C. botulinum* and the botulinum neurotoxin.

Low acid foods stored at ambient temperatures traditionally experience a severe ‘botulinum’ cook (heating at 121°C for 3 minutes or equivalent), and also establish a physical barrier to prevent post process contamination, to ensure that the probability of survival and growth of *C. botulinum* is negligible (most of the *C. botulinum* is destroyed by the thermal process and any residual spores from proteolytic *C. botulinum* are assumed to be non-viable over long periods). Improper application or unjustified moderation of the heating process, or failures of the integrity of the physical barrier to post process contamination, are identified with hazards.

In comparison with proteolytic *C. botulinum* and non-proteolytic *C. botulinum* other clostridia have only very rarely been associated with foodborne botulism. Limited laboratory data indicates that neurotoxigenic *C. butyricum* has heat resistance that is inferior to proteolytic *C. botulinum* and has a minimum temperature for growth in food that is equal to or exceeds that for proteolytic *C. botulinum*. A small amount of data indicates that, in the presence of organic acids, the growth of neurotoxigenic *C. butyricum* is also less acid resistant than growth of proteolytic *C. botulinum*. Consequently, foodborne hazards associated with formation of neurotoxin by *C. butyricum*, and potentially those associated with other clostridia such as neurotoxigenic *C. baratii*, can be aggregated with corresponding hazards that are identified with proteolytic *C. botulinum*. Present limited information about neurotoxigenic *C. sporogenes* suggests that corresponding hazards can also be aggregated with those associated with

proteolytic *C. botulinum*. This aggregation potentially contributes additional uncertainty to risk assessment.

6.2 Botulism - hazard characterisation

Foodborne botulism is a serious intoxication, affecting the human nervous system, which follows consumption of even very small amounts of neurotoxin that has been pre-formed in food (details of the disease are included in the Introduction of this report). Symptoms can arise a few hours post exposure but alternatively may be delayed by several days. Rapid clinical diagnoses, prompt administration of suitable anti-toxin and, in severe cases, respirational support are essential to remediate disease. The effects of foodborne botulism may persist for many months or years and can be life changing.

A systematic review of the effects of treatment on the mortality, hospitalisation rate and adverse effects from botulism[259] found evidence in relation to infant botulism and other evidence in relation to foodborne botulism. The evidence indicates that the use of trivalent anti-toxin to treat foodborne botulism had significant benefits in terms of mortality and hospitalisation if administered within 24hrs of symptom onset but the effect was reduced by delay (the review also indicates some side effects of treatment such as increased hypersensitivity reactions). In the UK treatment of botulism now involves administration of heptavalent antitoxin.

Botulinum neurotoxins, and their complexes, are relatively stable in foods and are believed to survive gastric passage unchanged. Toxicity tables expressing variability between different botulinum neurotoxins have been reported[260]. Botulinum neurotoxin type A1 is identified as the most potent human toxin, by intraperitoneal injection in mice, and type A neurotoxin has often been associated with the most severe human illness[30]. In the USA type F botulism has been most strongly associated with non-infant mortality[261] and mortality increases with age. However, consistent relationships between the onset or duration of illness and the dose or type of toxin have not been established so that differential diagnoses and treatments are problematic.

Botulinum neurotoxins are heat sensitive. Historic research indicates that, under laboratory conditions in buffer, botulinum neurotoxin types A, B, E and F, are inactivated after heating at 80°C for a few minutes[262]. However, following concerns relating to bioterrorism, additional research involving neurotoxins type A and B, and their respective protein complexes, indicated that inactivation by

more than 99.5% in milk was achieved following high temperature short time pasteurisation at 72°C for 15 seconds[263]. The thermal destruction of botulinum neurotoxins in complex food matrices using domestic cooking appliances remains uncertain and cannot be considered as an effective control with respect to foodborne botulism.

6.3 Foodborne botulism – UK exposure

Subsequent to publication of the 1992 ACMSF report there have been very few reports of incidents in which UK consumers were exposed to botulinum neurotoxin in food (Chapter 4 of this report includes details of UK botulism). The list of UK exposures includes incidents that involved chilled foods as well as incidents that involved foods intended to be stored at ambient temperatures so that for both hazards, independently, the frequency of occurrence can be classified as very low. In the UK botulism events are small and sporadic so that an annual rate is useful but volatile and could change rapidly following a large event. In the UK all reported exposures to botulinum neurotoxins in food, which have been identified with a confirmed source, have been associated with proteolytic or non-proteolytic *C. botulinum* (and in one case neurotoxigenic *C. sporogenes*). Other neurotoxigenic clostridia have not been associated with exposures in the UK but, since 1992, *C. butyricum* and *C. baratii* have been confirmed as the cause of food exposures in a small number of incidents in Europe and elsewhere. Clostridia other than *C. botulinum* cannot be excluded as a source of botulinum neurotoxin in food and so the frequency of occurrence, for the corresponding hazard, is also classified as very low. When compared to the accumulated volume of food consumed in the UK, which has capacity to support germination and growth of neurotoxigenic clostridia, the rate of exposure to botulinum neurotoxins per consumption event is exceptionally small.

The small rate of exposure extends over an increasingly wide variety of foods consumed in the UK that are potential vehicles for botulism. Very small exposure of UK consumers with respect to foodborne botulism is largely attributed to good hygienic manufacturing, adherence to recommended controls and systematic implementation of risk management procedures and practices, using HACCP principles, by food business operators.

Quantitative estimates of exposure for *C. botulinum* combine statistical evidence concerning spore loads in food materials with predictive microbiological models for spore inactivation and for germination, growth and toxin formation in food storage conditions. The modelling process can support risk management and

product developments but requires specialist expertise within a broader structured approach in order to be included into food safety decision making (the multi-agency SUSSLE projects are one example[264]).

Mathematical models for exposure highlight important uncertainties and variabilities in the current understanding of risk for foodborne botulism. In addition to the (reducible) statistical uncertainty that is associated with the values of model parameters there are deeper uncertainties that stem from (i) grouping of food materials into homogeneous classes (ii) the effect of process history on the subsequent behaviour of spores in food (iii) the effect of food chemistry, particularly the presence of lysozyme or other lytic enzymes[10], on the survival and recovery of spores during food storage and processing (iv) the possible unaccounted dependency between heat resistance and germination of individual spores (v) the precise relationship between cell growth and toxin production for *C. botulinum*. Research that integrates molecular information into quantitative modelling, and centres on the coordination of regulation for sporulation and toxin production pathways of spore-forming bacteria including *C. botulinum*[160], has begun to address some of these issues.

There are no published mathematical models that relate to germination, growth and toxin production for neurotoxigenic *C. butyricum* or *C. baratii* although some modelling approaches have used data collected from non-toxic surrogates for proteolytic *C. botulinum and* non-proteolytic *C. botulinum*.

6.4 Risk characterisation

Outbreaks of foodborne botulism have been reported worldwide for more than a century[30]; for incidents that involve two or more linked cases the median outbreak size corresponds with three cases and most outbreaks originate from point sources (consumption in one place at one time). The largest reported outbreaks have been associated with commercial food production and with multiple (complex) exposure events. Outbreaks for which there is strong evidence identifying a source are dominantly associated with *C. botulinum* producing neurotoxin types A, B and E. In a list of reported incidents of foodborne botulism (Table 4 in Chapter 4 of this report) failure to control storage temperatures is the most common confirmed cause and failure surrounding home canning of vegetables is also a common pattern; the list of reported incidents includes multiple records associated with smoked fish and type E neurotoxin from non-proteolytic *C. botulinum* but the data do not support the estimation of statistical significance for any of these causes. Other identified causes include

poor control of pH and water activity.

The 1992 report identified a particular hazard “specifically … the consumption of chilled foods in which the growth and toxin production by psychrotrophic strains of *C. botulinum* may have occurred before the food is perceived to be spoiled. The foods most at risk are those in which the spoilage microflora are eliminated or inhibited whilst psychrotrophic *C. botulinum* may survive and grow”. In a list of incidents involving botulism and chilled foods (Table 5 in Chapter 4 of this report), only a single case, involving vacuum packed smoked salmon that was consumed beyond the Use By date, and where temperature abuse was not reported, can possibly be identified with this hazard.

Evidence from outbreaks suggests that some mild cases of botulism may be underreported[27,30], either misdiagnosed or unascertained. In the United States[74] approximately 50% of cases of botulism in adults are diagnosed correctly prior to outbreak recognition. In the UK it is possible that some mild sporadic cases of botulism are undetected but observed incidents of foodborne botulism are all classified as public health emergencies and are reported in detail, at a national level, by an incident management team. Uncertainty associated with the assessment of the frequency of occurrence, and with the assessment of severity, of foodborne botulism is low (solid and complete data; strong evidence in multiple sources).

In the UK foodborne botulism is characterised by infrequent, isolated but serious events in which an individual, or a small group, are exposed to toxin during consumption or preparation of food. A clinical diagnosis of botulism is the trigger for coordinated multi-agency activity involving clinicians, epidemiologists, public health experts and, in the case of foodborne botulism, food manufacturers and food regulators. The response aims to minimise the case severity, rapidly identify additional cases and those at risk, track and trace all the potentially contaminated foods and remove it from the market, and ultimately limit the size of the event. The effectiveness of the response to an incident involving botulism is crucial to the reduction of risk (restriction of the event size for each outbreak and reduction in the number of incidents both contribute to the reduction of risk). Such is the potential severity of foodborne botulism outbreaks that product recalls are initiated immediately if a failure in commercial processing is suspected or known.

In relation to foodborne botulism, an appropriate level of preparedness should include a widely established suspicion and awareness of botulism among clinicians in order to increase the probability of early detection. In addition an

effective response requires sufficient accessible medical resources including epidemiological and laboratory support and the incident management team should be able to access exhaustive, real time, traceability systems for the relevant food products. In many countries a steady increase in preparedness, particularly rapid access to supplies of anti-toxin, has contributed to a declining case fatality rate for botulism. The investigation of a widely reported incident of foodborne botulism in Scotland during 2011[18] pointed to significant benefit from multi-agency coordination, time savings obtained by using real time PCR to detect botulinum neurotoxin encoding genes in environmental samples and to some inconsistencies in formal notification processes.

A review of outbreak investigations in the United States[74] highlights epidemiological linking of the earliest cases as crucial in expediting control over dispersed foodborne botulism incidents. This places emphasis on accurate early diagnosis and on rapid active case discovery. Botulism incidents that lack significant spatial or temporal clustering, such as those that might occur from foods with long shelf life, from foods designed for individual consumption, from foods that involve off site (“dark”) or unidentified production elements, from foods with dispersed or individual distribution patterns or from consumption settings where misdiagnosis may be more likely, may compromise case linkage, delay outbreak recognition, and present the most significant risks.

Since 1992 there have not been any clearly discernible trends in the occurrence of foodborne botulism in the UK. It is noted however, that the majority of incidents since 1992 have been associated with imported, home-produced foods and that there has been an apparent increase in global outbreaks associated with temperature abuse of chilled foods. Treatment of individual cases of disease, and linking cases with food and environments, has improved substantially as part of a move to a dominantly molecular scientific approach.

The successful control and the established decision-making framework for botulism safety in the UK is potentially challenged by emerging priorities for food manufacture. Reduction in energy use, reduction of waste (United Nations Sustainable Development Goals) and increased awareness of environmental concerns can manifest as reduction of preservatives, reduced packaging, radical new sources for food ingredients (e.g. meat replacements) or extended periods for acceptable use. In turn, the emergence of unexpected patterns of foodborne botulism cannot be dismissed. A move towards smaller scale, even individual, facilities for food production such as the increasing popularity of ghost kitchens and home canning presents concerns[265]. Home prepared foods, such as herbs

and spices or vegetables or mushrooms preserved in oil, and other small scale (unregistered) production, are less likely subject to rigorous controls relating to food safety and may include unpredictable and unrecorded distribution. Botulism risk associated with home and commercial bottling of vegetables in oil has previously been considered by the UK ACMSF[266].

In the UK, the control of foodborne botulism is moving into a complex multi-objective decision space that is part of the current development of UK food manufacture, delivery and use.

6.5 Conclusions

6.5.1 Controls

In the UK, established controls designed to prevent foodborne botulism, and the corresponding FSA guidelines for food manufacturers, are based on science.

Accumulated evidence indicates that for chilled foods, commercially manufactured in the UK and correctly stored at temperature not exceeding 8°C and consumed before the Use By date, existing controls act to maintain safety with respect to botulism. In addition, there are examples that suggest that the current FSA guidelines, and particularly the use of “a combination of heat and preservative factors which can be shown consistently to prevent growth and toxin production by non-proteolytic *C. botulinum*” or an updated statement that does not prioritise heating, include sufficient flexibility to support innovation by food business operators that can lead to reduced energy usage, waste reduction and safe shelf-life extensions. However, this may require significant financial investment and may not be accessible to SMEs in the industry.

Evidence continues to show that traditional low acid foods that experience a valid botulinum cook or other valid preservation step are exceptionally safe with respect to botulism. Currently it can be assumed that the controls aimed at prevention of hazards from *C. botulinum,* in foods that are intended to be stored at ambient temperatures, are effective for controlling hazards that could be associated with other neurotoxigenic clostridia. It is not clear that appropriate controls, or the application of a valid botulinum cook, can be guaranteed for low acid sealed foods produced outside of commercial manufacturing environments.

6.5.2 Incidents

Since 1992 there have been only a small number of reported incidents of foodborne botulism in the UK.

For chilled foods, the reported incidents of botulism are dominated by incorrect home storage of food at temperatures exceeding 8°C. For low-acid foods that are intended to be stored at ambient temperatures in cans or sealed containers, the majority of reported incidents involve an incorrect (non-commercial), or absent, heat treatment or alternative valid preservation step (often for food sourced from outside the UK by individual consumers).

The majority of reported incidents of foodborne botulism identify proteolytic *C. botulinum* as the causative agent, for foods intended to be stored at chilled or ambient temperature, although for some incidents involving type B neurotoxin the associated bacterium is not reported.

Investigations of recent UK incidents point to a system for effective multi-agency response to small, point-source outbreaks of botulism. It is not clear that current levels of preparedness with respect to foodborne botulism extend to include risks associated with small scale production or online distribution of food.

6.5.3 Trends

Since 1992 reported incidents of foodborne botulism in the UK have been small and localised with relatively routine epidemiological linkage of cases. Trends in food manufacture, particularly dispersed food distribution and individual food behaviours, as well as relatively large intervals between reported incidents, mean that a larger more dispersed incident cannot be ruled out and that preparedness is essential.

The science of *C. botulinum* continues to move forward and there are prospects for almost real time, high resolution, *in vitro* detection of botulinum neurotoxins and for improved, better characterisation of the biology and diversity of botulinum neurotoxin-forming clostridia, and mechanistic, understanding of stress response and toxin production pathways that can support next generation risk assessments.