ADVISORY COMMITTEE ON THE MICROBIOLOGICAL SAFETY OF FOOD INFORMATION PAPER

Risk-based considerations associated with consumption of human placenta

Background

The FSA carried out a literature review to evaluate scientific evidence that can be considered to develop consistent advice for Local Authorities and business involved in preparing/providing placenta intended for human consumption. The FSA requested comments from the ACMSF newly emerging pathogens subgroup on the literature review and risk-based comments relating to the consumption of human placenta and its products. Members evaluated the review and provided comments in writing focussing on six specific questions of interest to the FSA. A meeting of the subgroup was held on 11th January 2019 to finalise the subgroup's conclusions and discuss any further considerations; a record of meeting attendance can be found at Annex A.

From the outset, it was agreed that the group was not tasked with carrying out an external review for the FSA, rather, providing risk-based comments. The chair introduced the literature review highlighting the main points. The remainder of the meeting focussed on six specific questions relating to the risks associated with consumption of human placenta.

Specific risk-based questions relating to consumption of human placenta

1. **If you're aware of any other risks associated with consuming placenta, if the hazards mentioned pose a real risk, or if they are unlikely to cause harm.**

Microbiological hazards and issues

a. The literature review was well received by members and additional references were also suggested by members for inclusion in the review which can be found in the full set of members comments.

b. Members commented that raw, fresh placenta is an exceptionally good environment for microbial growth. It is neutral pH, high water activity, rich in nutrients and as such is unlikely to be inhibitory to most microorganisms. Members stated that it would seem reasonable to assume that the growth of bacterial pathogens can occur quickly in fresh placenta, the most significant factor being temperature and time. This may include growth of infectious and toxigenic bacteria. Bacterial growth is minimised if chilled within 4-6 hours.

c. There was agreement amongst members that microbial contamination of placenta would seem feasible either as a consequence of infection prior to birth or due to cross contamination with microorganisms from the mother or environment during birth.

d. Written comments from members highlighted that a number of recent studies have reported the detection of bacteria in placenta. The potential risks associated with the qualitative and quantitative details of such bacteria remain unclear, however, while this topic is currently under vigorous debate e.g. Zhu *et al*, and Taddei *et al*., it would seem reasonable to mention that the traditional concept - that the placenta is sterile - is currently under review.

e. At the teleconference, Members mentioned that the route of delivery (vaginal or trans-abdominal) will have an impact on differences in the microbial profiles of placenta samples. A reference, (Leon *et al*., 2018) was cited as evidence that could be included in the review to support this. Post cervical contamination vs caesarean delivery were discussed in terms of faecal and vaginal flora contamination of placenta. Written comments highlighted that faecal organisms including faecal pathogens are potential hazards depending on exposure during parturition and rapidity of chilling. Viruses and parasites such as *Toxoplasma* were flagged up as being potential hazards. Toxoplasma was viewed to be a problem if a susceptible pregnant woman mistakenly ate placenta contaminated with this parasite (under conditions of inadequate security and handling of this material e.g. mislabelling etc, discussed further below). Spoilage organisms were also acknowledged as being worthy of consideration.

f. Members expressed significant concerns relating to the potential for cross-contamination during handling and preparation of placenta and its products. It was stated that it is likely that all the placenta preparation processes present opportunities for additional contamination. It would be reasonable to assume that the rates for contamination by food handlers, environmental contamination such as the kitchen environment etc. are commensurate with other food business operations. Members were aware that the literature review also indicates that none of the processes used for preparation of placentae is likely to remove contamination completely. In this case it was viewed that the consumption of placenta could represent a real risk. There was a consensus view that it is likely that smoothie preparations provide the weakest hurdle for overall microbial growth (survival) and also amounts to the most significant exposure (assuming that it corresponds to a single consumption event). Members mentioned that the long shelf life of dehydrated encapsulated materials may also represent a significant risk if it can be shown there are pathogens that can grow or survive at very low water activity; particularly where host immunity to the pathogen was of short duration.

g. Members were concerned about the implications that may arise if placental products for human consumption were mislabelled or attributed to the wrong donor which could result in contaminated placenta being eaten by another potentially susceptible pregnant woman.

h. It was discussed that most ACMSF risks are identified with a pathogen and an exposure route, but in this case, no particular pathogenic agent is being considered, rather a community of bacteria in equilibrium with the host. Once removed from the host that community/microbiome is likely to change. In the period post birth, when there is cooling and other changes associated with the placenta material, it is possible that the microbiome (composition balance) could change significantly. If this evolution involved the decay of some sub-populations and the growth of others (driven by the lack of competition etc.) the appearance of a more hazardous microbiome cannot be excluded (although members were not aware of any evidence to support this scenario) and a new risk would arise. Since the material is cooling throughout this period those bacteria that have optimal growth below 37°C may also be favoured irrespective of competition effects.

i. Members noted that while it is reasonable to view placenta as meat for the purpose of the development of advice, it might be worthwhile considering it as a "temporary organ" not as voluntary or involuntary "muscle" tissue. Members viewed that it is sensible that advice should be based on the current food safety regulations for (collection, treatment, storage, etc) "offal" rather than "red" or "white" meats. The group expressed that there are more stringent requirements for offal handling than those for skeletal muscle.

<u>TSE hazards</u>

j. Oral exposure to prions was also discussed by members. It was viewed that although this is likely to be a theoretical risk, it should still be noted. A point was made relating to the assumption that if a woman is already infected, consuming an infected placenta will not be important in the context of that particular hazard, because she is already exposed to the infectious agent. However, if the exposure route alters, i.e. from another route to oral exposure, it was questioned whether this would make the woman more susceptible to a clinical illness from placental infection. This was discussed with a focus on prion disease. Prions are heat resistant and oral exposure is a likely route of exposure to prion diseases, though it was acknowledged that placental material is not normally considered a risk for prion disease, but it is not normally eaten. This issue was discussed both in terms of the consumption of one's own and someone else's donated human placenta.

<u>Chemical and physiological hazards</u>

k. There was a brief discussion on chemical hazards particularly highlighting opioids, with a view that placenta should not be consumed following a general anaesthetic as it may have absorbed opioids and other anaesthetic agents. Written comments provided by members also highlighted cadmium as a potential hazard. Smoking during pregnancy increases the concentration of

cadmium in the placental tissue and therefore also poses a risk via ingestion. Written comments provided by members also stated that the intake of placenta preparations in the presence of mastitis and/or blocked ducts is contraindicated due to the stimulating effect on milk production. Additionally, it was stated that estrogens in placenta may increase risk of thromboembolism especially in postpartum period.

Ethical issues

l. Consumption of a donated human placenta vs consumption of one's own placenta were mentioned in terms of concerns relating to security for handling and distribution of placenta and its products. Members expressed concerns relating to the possibility that if placentophagy were to be viewed increasingly favourably within society, that the likelihood of donations of placenta may increase and products may be consumed in a manner similar to vitamins etc. It was generally viewed that a donor placenta poses more risk than consumption of one's own placenta.

Other exposure pathways

m. Members highlighted that the literature review indicates hazard pathways from the consumption of contaminated placenta by a woman leading to infection of her breast feeding infant or to hazards for an embryo during subsequent pregnancy. One documented case concerning *Streptococcus* is evidence that this is a real risk but it is not clear how this risk is separated from the consumption of any other contaminated food by a mother (unless it is possible to identify a special class of pathogens that exclusively occupy this pathway). Members stated that this apparent observation may be associated with the under-developed gut flora of infants.

2. Do the hazards pose a real risk?

a. Members stated that for the simplest case (a woman consuming her own placenta after ideal handling and no external contamination) it is not clear that there is an actual exogenous exposure event. Most individuals have endogenous exposure to body tissues/fluids continuously and the consumption of a placenta is probably higher volume but otherwise no different. Without identification of exposure it would be difficult to identify risk. However, there was concern related to if the material becomes contaminated during handling or preparation etc., or if loss of controls results in consumption of a foreign placenta, that there is a real risk that can probably be considered similar to those from meat consumption (albeit with a highly distinct bacterial load). However, members highlighted the need to differentiate placenta processing from other meat processing which is discussed further in paragraph d below.

b. Members agreed that the chain of controls for placenta will not be perfect i.e. from delivery after birth through to the food product at ingestion, so there are real risks. As there are high levels of uncertainty on information and data around derivation, downstream handling,, stringency of identification and controls, immune status and disease status of the placenta for each case, then the natural hazards associated with any offal can be considered to be a real risk.

c. The issue of consumption of one's own placenta was further discussed in terms of whether contaminants that have originated from the mother i.e. endogenous infections are a real concern for that mother. Members considered that endogenous infections of the placenta do pose a risk, particularly to the new born baby as mentioned above. However, there was unanimous agreement that the highest risk would be associated with donor placenta that may occur as a result of loss of custody and stringency in the handling and preparation process; *Toxoplasma* infection was highlighted as being of particular concern in this context.

d. Members expressed that, in processing of placenta products for human consumption, there is a reliance on stringent infection control measures by the external processor and full sterilisation between each placenta. While members acknowledged some general similarities with the general meat processing, it was flagged very clearly that the level of control to prevent cross-infection between human placentas will need to be much more stringent than that usually employed by other meat processing procedures. Therefore, the point needs to be made that any risk assessment made on this issue is only valid if strict sterilisation procedures between each placenta are in place.

3. **Are immunocompromised individuals at greater risk if consuming***:*

-steamed (at 70°C for 2 mins) and dehydrated capsules
-dehydrated capsules from raw placenta (8 hours minimum, 55°C)
-raw placenta smoothie – prepared and consumed within 24 hours of delivery. Chilled within 30 minutes of delivery; temperature logged at 8°C 4 hours post-delivery, or higher if within 4 hours

a. It was noted that raw placenta could harbour microbial pathogens, including those that can be transmitted by consumption. Members stated that immunocompromised individuals are at greater risk than immunocompetent individuals, in consuming any material containing bacteria.

b. Members agreed that steaming would be the most effective method of reduction of microbial contamination but would not result in sterilisation. Drawing a parallel with offal/meat, it was noted that none of the above methods are likely

to render the solid or comminuted placenta sterile. It was stated that if this material was compared to a ready to eat (RTE) food, an effective cold chain and hygienic practices will extend the shelf life (i.e. prevent microbial growth) but will not deliver significant reductions in bacterial numbers. The difficulties in this area are confirmed by the current state of RTE foods, almost all of which are required to receive an effective thermal treatment (at some stage) to ensure consumer safety. Considering the immediate environment and activities around the collection of the placenta, it was stated that it would be prudent to specify an effective heat treatment (possibly, in the first case, by extrapolation from offal); however, it was acknowledged that this requirement may possibly face resistance along the same lines of consumer preference for raw rather than pasteurised milk.

c. It was stated that steaming at 70°C for 2 minutes would achieve a 6-log reduction in *Listeria monocytogenes* and a much larger log reduction in enteric pathogens such as *Salmonella* although that would be in high water activity foods and the information seems to indicate this may happen during / at the end of drying which would have a marked reduction on lethality. It was noted that the efficacy of these temperatures on viruses and parasites is less clear although some of the data presented seems to indicate that reductions would occur.

d. Members stated that heat processing to 70°C for 2 minutes is a recognised process for ensuring the safety of raw meat and could be equally employed for placenta.

e. It was noted that dehydration at 55°C would prevent the growth of most bacterial pathogens (once dried) although spore formers such as *Clostridium perfringens* may present a potential risk dependent on the management of temperature. Members mentioned that it should not be assumed that drying at this temperature would kill microbial pathogens as this may not be the case depending on how it is done.

f. Members viewed that though steaming was the most preferable approach listed, there was a general unease about recommending it. Smoothie products were unanimously regarded as the riskiest approach with the highest uncertainty. It was acknowledged that some hazards such as prions would not be affected by heat. Members stated that it is difficult to simply review methods of contamination without suggesting methods of decontamination.

g. It was noted that smoothie preparations is likely to provide the weakest hurdle for overall microbial growth (survival) and also amounts to the most significant exposure (assuming that it corresponds to a single consumption event). The long shelf life of encapsulated materials was also mentioned possibly representing a significant risk if it can be shown there are pathogens that can grow in very low water activity.

h. Members mentioned that in terms of consumer behaviours and perceptions, there will likely always be some people who will prefer to consume the raw products for whatever reason in a similar way to raw drinking milk, so members viewed that they needed to be quite definitive in describing the efficacy (or not) of these treatments. It was also acknowledged that the effectiveness of these approaches will be determined by the level of process control management, so will not provide complete reassurance.

i. It was acknowledged that, the (current minority) demand for placenta consumption make safe hygienic collection, processing and return of the right placenta to the correct consumer logistically more difficult than “normal food processing” (where all “the product” goes through the same processes).

4. How could failure to adequately chill affect growth of bacteria in the first 4 hours?

a. It was noted that pathogenic bacteria could proliferate in placenta if inhibitory factors are not introduced i.e. chilling to <8°C within 4-6h; drying; acidification; or limiting shelf life.

b. It was acknowledged that in general terms, the onset (continuation) of microbial metabolism and multiplication in such cases is modulated by the severity of the changes in the environment facing bacteria, therefore, significant changes in temperature, pH, etc would result in a requirement for bacteria to carry out many internal metabolic adjustments before beginning to grow and multiply. Some modelling using meat or offal under delivery room conditions could be carried out. As in many cases, comminution of placenta is likely to protect initially surface-restricted contaminating bacteria within the minced material.

c. Members stated that temperature particularly but also other environmental conditions prevalent at the time before chilling such as pH, humidity etc would impact on microbial growth and this would depend on level of endogenous bacteria and faecal contaminants etc being introduced in the delivery process. Members however, were in agreement that the question is very complex, given that a single species or strain with known kinetics is not being dealt with but rather a microbiome. Members noted that some bacteria may be present on placenta with optimum temperatures for proliferations below 37 °C and others at 37°C and the placenta microbiome will change following removal from the body. Some bacterial species will not survive, and others may thrive, therefore resulting in changes to the microbiome; changes that may not be of benefit if growth of pathogens is favoured. It was expressed that predicting microbial behaviour in the presence of diverse and large communities of micro-organisms is impossible.

5. **How likely is it that visual inspection of placenta by a midwife will detect infection e.g. Chorioamnionitis?**

a. Members stated that many conditions can be missed on inspection of a macroscopically normal placenta. Midwifes have guidelines on inspection which have been established to ensure the whole placenta has been removed from the body, but these are not set to look for contamination. It was noted that inspection of placenta can miss not only infection, but also chemical contamination. Visual inspection will detect conditions associated with macroscopic pathology e.g. ischaemic damage due to prolonged infection. Members stated that although placenta may look macroscopically normal in chorioamnionitis, this may not be the case at the cellular or microscopic level and histopathological examination is advised in suspected cases of chorioamnionitis.

6. **What is the pathophysiology of retained products of conception i.e. placenta, and sepsis (how does RPOC bring about puerperal sepsis?)**

a. Members stated that RPOC are an ideal culture medium for bacterial growth within the uterus, usually the products become infected from ascending polymicrobial faecal flora (Gram negative bacteria and anaerobes) or staphylococci. Risk is worsened if there has been prolonged labour, instrumentation, tears etc. The postpartum mother is an immunocompromised host who can rapidly acquire disseminated infection, sepsis and disseminated intravascular coagulopathy (DIC). Treatment includes immediate evacuation of the uterine contents along with antibiotics.

b. Members stated that postparturient or puerperal sepsis is most often associated with faecal organisms. Members highlighted that an incomplete placenta could enter the food chain having originated from a woman entering into puerperal sepsis and be subject to higher levels of contamination than a healthy placenta.

Concluding remarks and further comments

a. Members concluded that there is substantial complexity and uncertainty that arises from endogenous hazards associated with placenta (bacterial, viral and parasitic) particularly where there is insufficiency of chain of custody of identity. Members also noted external contaminants that may be acquired post-collection particularly from vaginal delivery but also resulting from caesarean section. Members viewed that there is so much complexity and uncertainty of the placenta delivery and production process that it is very difficult to estimate the probability and severity of outcome even for what may be considered to be “home bacteria” or “home infections” from the mother of origin. This uncertainty is compounded by variations in the sufficiency of the mother’s own immune status but also that of the neonate that will be intimately associated with her over the period of time of consumption of the placenta.

b. Members also noted the possibility of unknown risks that may emerge and have not been considered by the group.

c. Members viewed that risks can be separated according to three distinct (unjoined) exposure pathways: placenta consumption by the originating mother, another individual consuming that placenta, or the infant involved with the mother who consumes her placenta. Members viewed it would be useful for the FSA to indicate that the risks are influenced by these three separate routes/scenarios.

d. Members also noted that it may be possible for a subsequently pregnant mother to consume preparations of placenta from her previous birth by way of capsules; this is more likely to occur if there is little time between the pregnancies and consequences for the foetus and for the mother, based on pregnancy associated immunosuppression, should be considered.

e. Members also noted the potential for occupational exposure in relation to the food business operators but acknowledged this was not within the group's remit.

f. There was a further discussion relating to uncertainty of the dehydration (desiccation) process of placenta. The possibility that dehydration of contaminated placenta might result in possibility of inhalation contamination via aerosol to handlers, mother, or infant and the kitchen environment was discussed. Members viewed that most desiccators function with partial vacuum that re-condenses to provide a liquid output rather than a vapour output, however this would depend on the way the desiccator functioned. Infectious particles would probably be contained in the liquid rather than be dispersed. However, there was concern relating to whether the equipment used in desiccation would be autoclaved after use as this was viewed to present a potential for cross contamination. Members viewed that there may be some potential risks and uncertainties arising from the dehydration process as the process of desiccation can be performed in different ways with different types of desiccator etc.

Annex A

Meeting of the ACMSF Newly Emerging pathogens subgroup was held by teleconference on 11 January 2019.

The membership of the group is as follows:

Chair
Dr Dan Tucker

Members
Dr Gary Barker
Dr Gauri Godbole
Professor Miren Iturriza-Gomara
Mr Alec Kyriakides
Dr Gwen Lowe
Professor David McDowell

Apologies were received from Miren Iturriza-Gomara and Alec Kyriakides (written comments provided).