### 1. Are there any additional types of human bodily material that could raise ethical concerns?

Asterand recognizes three types of collections of human biological materials:

(a) living donor collections
(b) post mortem donor collections
(c) third party or "archive" collections

Of these, living donor collections tend to involve the tissue types that carry the highest ethical concerns, particularly collections involving non-medically necessary procedures and interventions during the collection process (e.g. skin punch biopsies or induced sputum collection are typical examples).

### 2. Should any particular type(s) of human bodily material be singled out as 'special' in some way?

The following tissues should be treated as "special:"

(a) tissues with reproductive implications
(b) foetal/embryonic tissues
(c) tissues acquired via a non-medically necessary procedure
(d) tissues that are non-regenerative

Items (a) and (b) may come with specific regulatory and legal implications, e.g. law in Michigan, US, states that no woman may have an abortion for the purpose of donating tissue for medical research. All consent practices should take into account these different laws. The latter (c) and (d) come with unique issues as well, although certainly not as stark as those applicable to (a) and (b). With (c), the researcher is not just "riding alongside" a medical procedure, but may be dictating how and when that procedure will be performed (e.g. skin punch biopsies). Tissues that are non-regenerative are often treated differently as well, again because of governing laws and regulations. For example, the Mayo Clinic carves out this type of tissue because Minnesota laws state that only regenerative tissues may be "sold" for research use. Hence, blood collections are permissible, but surplus surgical are not. While these examples may be specific to the US, they may throw light on bioethical aspects worthy of consideration here.

### 3. Are there significant differences between providing human bodily material during life and after death?

Living donor and post mortem collections are distinct from an ethical, logistical and scientific standpoint, and should be treated as such. Living donor collections generally mirror clinical trials with respect to the way in which consent, ethical review and sample procurement are performed. Consent, ethics review and procurement for post mortem collections for research are often less consistent and overlap with the regulations and processes regarding transplantation.

**4. What do you consider the costs, risks or benefits (to the individual concerned, their relatives or others close to them) of providing bodily material? Please distinguish between different kinds of bodily material if appropriate.**

The risks of donation vary according to collection type and can be classified into physical and non-physical risks

Physical Risks

- Donation of surplus surgical tissues for research should pose no additional cost or physical risk to the wellbeing of the patient as long as diagnosis is not compromised - diagnosis is, and must always be, the priority.
- Donation of additional material, beyond that required by the medical procedure, can also pose minimal risk. However, additional ethical approval /consent to donate any additional materials (e.g. extraordinary blood draws) must be appropriately sought.

Non Physical Risks

- The non-physical risks include, but are not limited to, risk of loss to privacy, risk of publication of personal data within private, public or government databases, and risk associated with discovery of genetic information regarding heritable diseases etc (e.g. implications for insurance coverage, employment).

Benefits

- The benefit of altruistic donation is the knowledge that the patient / donor is facilitating advances in medical research.

**5. What do you consider the costs, risks or benefits (to the individual concerned, their relatives, or others close to them) of participating in a first-in-human clinical trial?**

For First in Human trials, there is a key difference in risk in that healthy volunteers risk suffering adverse effects or discomfort as they are administered a new drug in early clinical development. The risk of first in human trials is dependent on the quality of pre-clinical data and likelihood for such adverse events. These risks can be mitigated by relying on high quality human biomaterials based information, in addition to data from *in vitro*, *in silico* and animal models.

Subjects are not generally expected to derive any physical benefit from First in Human trials, but may receive benefits that are monetary or altruistic in nature, based on the degree of invasiveness of the trial, any associated risk to their well-being and the fact that these studies are mandated by the regulatory agencies.

**6. Are there any additional purposes for which human bodily material may be provided that raise ethical concerns for the person providing the material?**

Human biomaterials may be used to create derivative products, such as RNA, DNA, proteins, cell lines or tissue microarrays. This presents a situation where biomaterials from the same donor may be used for both immediate use and for future unspecified purposes, or may be used both commercially and non-commercially. Given scientific advancements in creating derivative products from human tissue, materials from a donor may continue to contribute to scientific research long after the initial specimen is "exhausted." This may pose ethical considerations for patients who may not have envisioned future uses for the derivatives. To address these concerns, it is important that where possible the consent form outline the possibility of unspecified future use for the material and provide adequate "opt-out" procedures for donors who wish to withdraw use of their specimen in the future.

**7. Would you be willing to provide bodily material for some purposes but not for others? How would you prioritise purposes?**

Asterand has not seen a significant distinction in patient perception and consent for commercial as opposed to non-commercial research purposes. Consent rates for surplus surgical tissues remain very high for all such research purposes, so long as the perceived goal involves the development of new diagnostics, prognostics or treatments for disease. Donors also have not appeared deterred by unspecified research uses.

**8. Would your willingness to participate in a first-in-human trial be affected by the purpose of the medicine being tested? How would you prioritise purposes?**

N/A

**9. Are there any other values you think should be taken into consideration?**

The value of autonomy must encompass full knowledge and understanding of the choice being made.

**10. How should these values be prioritised, or balanced against each other? Is there one value that should always take precedence over the others?**

Autonomy and Altruism should take priority, and, in practice, are much easier to conceptualise and enforce through processes. Concepts such as Dignity and Justice have proven ambiguous in practice and should be minimized. For example, Tissue Bank XYZ requests that client ABC sign a contract promising to treat all tissues with "Dignity." The Parties may differ completely in terms of what is considered "Dignity," whereas they will likely agree that donors should not be paid to donate tissue (i.e. altruism) and that donors must understand the nature of the donation they are voluntarily agreeing to (i.e. autonomy).

**11. Do you think that it is in any way better, morally speaking, to provide human bodily material or volunteer for free, rather than for some form of compensation? Does the type or purpose of bodily material or medicine being tested make a difference?**

No. However, introduction of a payment-for-participation component that exceeds reasonable patient stipend for travel and time may create an environment of "economic coercion" that may provide unfavourable incentives and outcomes for poor or socio-economically disadvantaged individuals.

**12. Can there be a moral duty to provide human bodily material, either during life or after death? If so, could you give examples of when such a duty might arise?**

We believe, individuals must be free to arrange for the disposal of their remains in accordance with their personal beliefs, values and religion. However, if default donation procedures are adopted to govern post mortem specimen donation, providing an "opt-out" mechanism should suffice to meet this need.

**13. Can there be a moral duty to participate in first-in-human trials? If so, could you give examples of when such a duty might arise?**

No.

**14. Is it right always to try to meet demand? Are some 'needs' or 'demands' more pressing than others?**

Demands that impact the largest patient population or those in critical need (e.g. for understanding rare diseases) should likely be prioritized, where such distinctions are clearly discernable.

**15. Should different forms of incentive, compensation or recognition be used to encourage people to provide different forms of bodily material?**

Current financial and in-kind reimbursement methods are sufficient.

Altruistic donation should be encouraged through increasing awareness and education of patients and hospital staff seeking consent re: importance of human tissues for research and development of new medicines.

In First in Human trials, volunteers are reimbursed for their involvement. These are regulated, mandatory studies that Pharma must perform to support registration of new drugs. The use of human tissues for preclinical research is not currently mandated. Once this changes, perhaps the incentives should be revisited to address the potential 'availability bottleneck' that could occur if certain materials become a requisite for progressing a new drug through to registration.

However, if tissue donation of any kind subject to significant financial reimbursement, there is an increased risk of creating a black market in human tissues / organs
http://news.sky.com/skynews/Home/Sky-News-Archive/Article/200806413560704

See also The Times, October 20, 2006 : The $1bn trade that is beyond the eyes of the law

**16. Are there forms of incentive that are unethical in themselves, even if they are effective? Does it make any difference if the incentive is offered by family or friends, rather than on an 'official' basis?**

Direct payment to a donor for human biomaterials should be discouraged other than for reimbursement of reasonable expenses relating to time and travel incurred.

**17. Is there any kind of incentive that would make you less likely to agree to provide material or participate in a trial? Why?**

No.

**18. Is there a difference between indirect compensation (such as free treatment or funeral expenses) and direct financial compensation?**

Yes. Indirect compensation is acceptable, particularly for post mortem collections, whereas direct financial compensation creates a free market in biomaterials and should be discouraged.

**19. Is there a difference between compensation for economic losses (such as travelling expenses and actual lost earnings) and compensation/payment for other factors such as time, discomfort or inconvenience?**

Depending on the circumstances, either compensation would be acceptable.

**20. Are you aware of any developments (scientific or policy) which may replace or significantly reduce the current demand for any particular form of bodily material? How effective do you think they will be?**

Advances in the development of stem cell-derived human cells that fully demonstrate a native cell phenotype will inevitably impact the need for fresh human tissues in some areas in the future. However, this remains several years away. In the meantime, and going forwards we foresee increases in demand for human tissue for research purposes, in particular in areas where stem cell derived cells are not yet applicable (e.g. target / biomarker identification and validation in disease) or may not be able to be created / validated.

**21. In your opinion are there any forms of encouragement or incentive to provide bodily material that invalidate a person's consent?**

Any incentives that are not approved by an appropriate ethics committee, or any encouragement that rises to a level so as to be misleading to the prospective donor, may invalidate the donor's consent.

**22. How can coercion within the family be distinguished from the voluntary acceptance of some form of duty to help another family member?**

Coercion by definition involves force, generally accomplished by threats, intimidation or trickery. The presence of these components distinguishes from a duty to help, which would be more or less implied and arise from the relationship

itself. The use of appropriately trained consent staff should help ensure a subject has not been inappropriately influenced by family.

**23. Are there circumstances in which it is ethically acceptable to use human bodily material for additional purposes for which explicit consent was not given?**
Yes. Where the human bodily material has been approved by an ethics committee for the proposed additional purpose, the re-consenting requirement may be waived. In addition, where tissues have been unlinked from the patient identifying information, their use should be permitted.

As described above (Q6) tissues may be procured with "general" intent where typically consent for research is quite broad, to allow for future research that may not be conceived of or feasible at the time of donation, e.g. due to lack of appropriate methods / technology advances. However, some may have specific use / restrictions applied at the time of collection, based on the IRB review and resulting consent form for a given collection.

Incredible scientific research value is locked up in archive tissue / biofluid collections and the scientific community should be able to realise this latent value as scientific breakthroughs emerge and technology rapidly advances.

One example of the importance of being able to apply new technologies to old samples is in the forensic arena where there is plenty of evidence to demonstrate the value for subsequent identification of, and dealing with, perpetrators of crime.

**24. Is there a difference between making a decision on behalf of yourself and making a decision on behalf of somebody else: for example for your child, or for an adult who lacks the capacity to make the decision for themselves?**
Only legal representatives or next of kin should be permitted to act on behalf of an incapacitated adult. Where the consent of a child is required, the child should sign an assent form to indicate their understanding of the procedure and risks (provided they are of an appropriate age, likely from around 7 years old). For children too young to give assent, the decision should rest solely with the child's parents or legal guardians.

**25. What part should family members play in deciding whether bodily material may be used after death (a) where the deceased person's wishes are known and (b) where they are unknown? Should family members have any right of veto?**
Family members should not be allowed to veto the deceased person's wishes, provided the deceased person gave clear intention and / or made arrangements for donation prior to their passing. However, where consent is acquired from the next of kin after the death of the prospective donor, or where there was not clear intention from the donor, the next of kin should have the full right to accept or decline donation of their family member's tissue and organs.

**26. To whom, if anyone, should a dead body or its parts belong?**

Various laws may place the custody and control of a dead body in the hands of medical professionals (i.e. coroner) or next of kin or legal representatives. Each of these individuals should have full authority to utilize or dispose of the body as they see fit, provided such actions are consistent with applicable laws and ordinances.

**27. Should the laws in the UK permit a person to sell their bodily material for all or any purposes?**

The laws of the UK should not permit a donor to directly sell their bodily materials, but should account for remuneration to the donor for time and travel involved in the donation process. In addition, compensation should be available for those who render services in relation to such donation process, or those that transfer, store, process, add additional characterisation to or dispose of the tissues that are donated.

**28. Should companies who benefit commercially from others' willingness to donate human bodily material share the proceeds of those gains in any way? If so, how?**

No. Many entities that perform commercial research rely on tissues provided by hundreds of distinct donors, and it is rarely if ever possible to compare or contrast the usefulness or research value of any one donation over the others or of the human tissue aspect of the research versus other aspects. In addition, these organizations bear the full cost of research failures in addition to the successes. Furthermore, to attempt to do so, would be genuine commoditisation of tissue, and would further present a disincentive for research. Sharing proceeds would inevitably introduce a bargaining component to the donation process, which would exponentially increase the already steep costs associated with the tissue donation and collection processes.

**29. What degree of control should a person providing bodily material (either during life or after death) have over its future use? If your answer would depend on the nature or purpose of the bodily material, please say so and explain why.**

A person should have control according to the terms set forth in the applicable consent form, except as noted for un-consented future research use (see above questions). This should include the ability to withdraw consent. Withdrawal of consent is a process that works, but in our experience is rarely actioned.

**30. Are there any other issues, connected with our Terms of Reference, that you would like to draw to our attention?**

No