13 Tissue Banks responded out of 88 possible (≈15%): 9 U.S. processors, 1 Canadian processor, 2 Recovery-only agencies, and 1 Reproductive bank. The Canadian bank’s responses are not used in this report since they do not distribute tissue to the U.S.. Using AATB’s Annual Survey information for 2003 that contained reports from all accredited banks, distribution activity was evaluated for that year, then banks ranked according to highest activity and compared to those banks that completed this new survey. This analysis was performed to evaluate how much of the U.S. tissue distribution activity (by accredited banks) was represented by the current response to the new survey (that covered two years: 2003 & 2004).

Listed in descending order of overall tissue type distribution activity (does not include semen or amnion):

- MS tissue (bone, bone+cartilage, demineralized bone) - ≈ 67% (1.23 million, this survey)
  7 of the top 12 banks

- Soft Tissue (tendons, ligaments, fascia, pericardium) – ≈ 52% (101,000)
  7 of the top 12 banks

- Skin - ≈ 29% (>25,000 sq ft)
  5 of the top 12 banks

- Vessels (veins, arteries) – ≈ 95% (7,200)
  3 of the 5 banks

- Cardiac (heart valves, conduits) - ≈ 61% (6,700)
  3 of the 5 banks

**“Suspected” Allograft-associated Infection Reports Received**

192 total patient reports

**Overall incidence of “suspected” reports is ≈ 0.014%**

Of these, incidence per graft type:

**Soft Tissue 42%**
- Bone 37%
- Cardiac 9%
- Vascular 7%
- Osteochondral (bone+cartilage) 4%

Of these, incidence per processing method:

**Aseptic (antibiotic disinfection) 49%**
- Irradiated (if at all, but not labeled sterile) 44%
- Labeled sterile 7%
Of these, operative procedure performed:
**Orthopedic/Sports Medicine 57%**
Neurological 15%
Cardiac 10%
Vascular 9%
Unknown/not reported 8%
Dental 1%

**Signs and symptoms** from reports of suspected allograft-related infection:
41 Positive culture (wound, aspirate, not specified)
12 Drainage (clear, serous, purulent, increased)
11 Inflammation, redness, swelling
7 Fever
5 Positive Serology (HCVx4, HBVx1)
4 Pain
1 each of these: Fatigue w/high titer IgG CMV, cellulitis, joint effusion, soft tissue atrophy, septic arthritis, non-union, graft rupture, graft deteriorated, endocarditis, pyogenic myositis

**Frequency of organisms** reported when “culture positive” (this information was freely offered, it was not specifically requested):
7 S. aureus (2 were MRSA)
5 S.epi.
4 “Strep.” (1 was “alpha”)
4 Enterococcus
3 Mycobacterium
2 each of these: “Staph.”, Serratia, E. coli
1 each of these: “Gram’s stain + (not specified), Propionibacterium acnes, Corynebacterium, Acinetobacter, Bacteroides, Enterobacter, Proteus, Pseudomonas, Aspergillus, Yeast, Candida, “unspecified”

**“Probable/Proven” Allograft-associated Infection Reports Received**
2 total patient reports
**Overall incidence of “probable/proven” cases is 0.00015%**

Common graft type, processing method, and application:
**Osteochondral, Aseptic/cryopreserved, Orthopedic**

Graft recalled/destroyed: 4 grafts recalled from field, 9 already implanted, 5 quarantined from undistributed inventory.

Testing performed: Recipient cultures (wound, archived serum), allografts cultured (both quarantined/undistributed inventory & recalled grafts)
Original Suspected Cases that were NOT Deemed Related to Allograft

Infection attributed to (in order of prevalence):
1. Unknown x 24 - investigation dropped by reporting entity
2. Nosocomial infection x 3
3. Improper OR prep of graft/culturing x 3
4. Superficial cellulitis x 2
5. Improper wound care x 2
6. x 1 each: break in sterile technique, surgical wound infection, pre-existing tissue infection, HCV due to occupational exposure, Hepatitis from blood transfusion suspected

Obstacles encountered by tissue banks when investigating reported suspected allograft-related infections (each bank’s comments are listed as one):
1. Lack of response to bank’s inquiries (not prompt); Pt's culture results not received for 5 weeks.
2. Delays receiving responses from physician's offices who were contacted to obtain information regarding symptoms of post-op infections in their recipients (of implicated donor's other allografts).
3. A checklist (requesting critical information) we send to the physician for completion is occasionally not returned. This contains info that can determine if FDA is informed of the suspected infection or not.
4. Reporting site's refusal to provide specific patient/event information (culture results, pathology reports, pt medical hx, details of clinical course, etc.)
5. Not being provided with a graft (serial) ID number related to the suspected infection; Not being provided culture reports and hospital investigation summaries in relation to an alleged adverse event.
6. Difficult to obtain follow-up documentation in a timely manner, if at all (pt status, culture results, surgery details); many times personnel reporting the infection are only vaguely familiar with case = many phone calls/case; Difficult to convince medical personnel that HIPAA does not apply in these cases.
7. Un-returned phone calls.
8. HIPAA Regulations - inability to obtain or access & review all hospital surgical and medical records surrounding the immediate event.

Estimated cost to tissue bank related to investigating “suspected” allograft-related infections: Low of $100 to high of $100,000 (average $1,239 to $21,750). Costs mostly attributed to personnel time, then operational/shipping costs (related to recall); grafts being destroyed; and testing costs (in-house & contracted). Loss of business was not calculated into these costs so would be ‘in addition to’.

Proposed Definitions

Suspected: Most agreed but requested that changes be considered. Comments listed by each bank are grouped as one:
1. Many of these symptoms could also be associated with infections caused by the surgical procedure.
2. Time frame of one year for bacterial/fungal infections is too long; suggest 3 months; it is the close relationship in time between allograft implant to onset of symptoms that raise suspicion of allograft-related infection. Change "positive culture from deep within operative site" to "positive wound culture" since surgeons often culture purulent discharge. Reword Blood Cultures to define that they must be truly positive (not skin contaminants).
3. Delete “lymphadenopathy.” Change "one year" to "3 months".
4. “One year” may be too long, suggest 6 months since bacterial/fungal infections should present within this time and HCV has a long window period of about 6 months; using a year increases potential for recipient to experience conditions/disease exposures contracted well after implantation that are unrelated to allograft.
5. Need to consider use of adjunct hardware (e.g., staples, interference screws, etc.). These are putative sources of infection.
6. One year post surgery is too long.
7. One year post surgery is way too long (suggest 8 weeks); Positive Blood Cultures not necessarily related to allograft.
8. For Reproductive tissues, there is an additional need to include testing of sexually intimate partners (casual and/or long term) of the recipient.
9. May want to specify "confirmed" in Parasitic/Viral "b.

**Probable:** Most agreed but requested changes be considered. Comments listed by each bank are grouped as one (some redundant from above):

1. A match of the bacterial/fungal culture findings does not necessarily give a probable qualification if the organism(s) is (are) commonly found in the environment.
2. Bacterial/Fungal: Use "A match between the culture findings of an uncommon organism isolated from the operative site in a recipient with no identified risk for the disease with culture findings on pre-processing, in-process, or final cultures of any tissue from that donor." (e.g., Propionibacterium found on both would not indicate it is allograft related). Also use "Report of allograft-associated infection with the same organism as in the original adverse event report in other recipients of tissues from the same donor.
3. Bacterial: May need a provision for occurrences of common organisms found within surgical ORs/hospital settings and recognized as skin contaminants.
4. Need to consider use of adjunct hardware (e.g., staples, interference screws, etc.). These are putative sources of infection.
5. Bacterial/Fungal: Must document how cultures were obtained, stored, shipped, who analyzed and how, to be of use.
6. For Reproductive tissues, there is an additional need to include testing of sexually intimate partners (casual and/or long term) of the recipient.
7. May want to specify "confirmed" in Parasitic/Viral "a."
Proven: All agreed (100%). There was one comment:
1. So much depends on the laboratory test and technique that without qualifying the above statement one cannot (entirely) agree as it is written.

Do You Recommend Culturing the Allograft Prior to Use?
No x 9 ; Yes x 4
Comments listed by each bank are grouped as one:
1. Culturing of a sterile product opens the product to accidental exposure to contamination.
2. It is possible to contaminate the graft or the culture by a break in sterile technique after the graft has been removed from its packaging. This additional culture information is of little value. A negative culture does not mean the allograft is sterile. Additional patient cost.
3. Many false positives causing unnecessary use of antibiotics for the patient.
4. Methods used to culture allografts in the OR setting are not standardized or validated so risk of false positives is considerable. Culturing methods can damage or contaminate the allograft. Leads to unnecessary use of antibiotics for patients.
5. Swabs done in the OR are useless (low specificity/sensitivity), are prone to (overt) contamination, and often un-interpretable. No need to culture a sterile graft (sterilized by a validated process).
6. When gram stain done and shows organisms, this does not prove organisms are viable. Risk of graft being contaminated by procedure in OR.
7. Frequently, allografts are re-shaped by surgeon so this must be documented. Also, wound/implant site must be cultured before and after implant for any value.
8. Not applicable to semen.
10. Would help in determining infection source.
11. In our experience, positive allograft cultures taken in the OR are not linked to the allograft but are due to poor culturing techniques used by the implanting institution.
12. In the event of an infection or positive pre-op surgical culture, one may ascertain the probability of the donor graft being the infection source. However, it may be unnecessary with validated sterilization methods & validated packaging methods. In any case, it is an asset for liability defense & protection.

Additional ID #
Advantages:
1. Tracking adverse events to one donor may be easier.
2. Ease of communication between tissue banks and (recovery agencies) regarding shared donors (could help meet 21 CFR 1271.160(b)(2)).

Disadvantages/Comments:
1. There is no problem tracing by our own identification number.
2. Logistics involved to create such a system (more than one tissue recovery agency involved all needing number prior to beginning recovery after acceptance of donor). Just another cross-reference # adding no value. Requires additional cross-reference in records or new # to appear on label.
3. Ability to provide one number to all parties involved may not be practical. Matching and referencing an additional number may pose burdensome to some organizations.
4. Current system working well; additional number would require costs and time (computer program changes, additional staff training, labeling changes, SOPs).
5. No system in place to support it.
6. Who will pay for it and track this?
7. Current ID system is working.
8. Who would manage system? When would number be assigned? Just another number to track. Only useful if processors use this instead of assigning their own.
9. Do not understand the benefit of an additional number.
10. Multiple IDs create possibility of donor confusion. Tissue banks may also have numbering systems that are tailored to meet their needs.

Bar Coding
Used for donors? No x 8; Yes x 4 Used for allografts? Yes x 6; No x 4
ISBT 128 planned? No x 5; Yes x 5; Undecided x 2 Comments: ISBT 128 not a high priority but great idea; Bar coding used for internal tracking only

Virtual Tissue Repository
Advantages
1. The availability could be useful in some investigations.
2. Trace-back opportunity.
3. Re-testing of tissue.
4. Additional tracing number.

Disadvantages/Comments/Questions (grouped from most often mentioned first).
1. Storage/Equipment/Space limitations (physical storage burden).
2. How would you handle repeat semen donors?
3. Cost.
4. Questionable usefulness.
5. Appropriate sample size difficult to establish.
6. Intent is for pre-processing archive or post-processing archive, or both?
7. Access (under contract processing -which bank retains samples?).
8. Condition of material over time would need validation.
9. Additional tracking systems/SOPs needed.
10. Can currently use other means to accomplish same result through investigations.
Reference Request (other than MMWRs)

AAMI, ISO  *(but no specific publications given)*