

Processed “Conventional” HCT/Ps and Low Risk for Chagas’ Disease

Blood Products Advisory Committee Meeting
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Chief Policy Officer

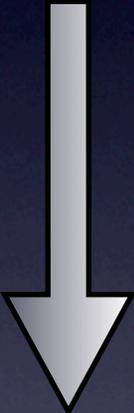


AATB

- Founded in 1976
- Professional, non-profit, tax exempt, scientific and educational organization
- Authoritative *Standards* since 1984
- Voluntary accreditation offered since 1986
 - ▶ 98 accredited tissue banks (US and Canada)
 - ▶ Annually, they recover \approx 25,000 tissue donors & distribute \approx 2 million grafts
- Certification exam for technicians since 1987
 - ▶ Certified > 3,000 CTBS's worldwide

“Conventional” HCT/Ps

FDA List:

- 
- Bone
 - Skin
 - Tendon
 - Ligament
 - Fascia
 - Pericardium
 - Heart valve
 - Vascular graft
 - Amniotic membrane
 - Cartilage
 - Dura mater

AATB designations:

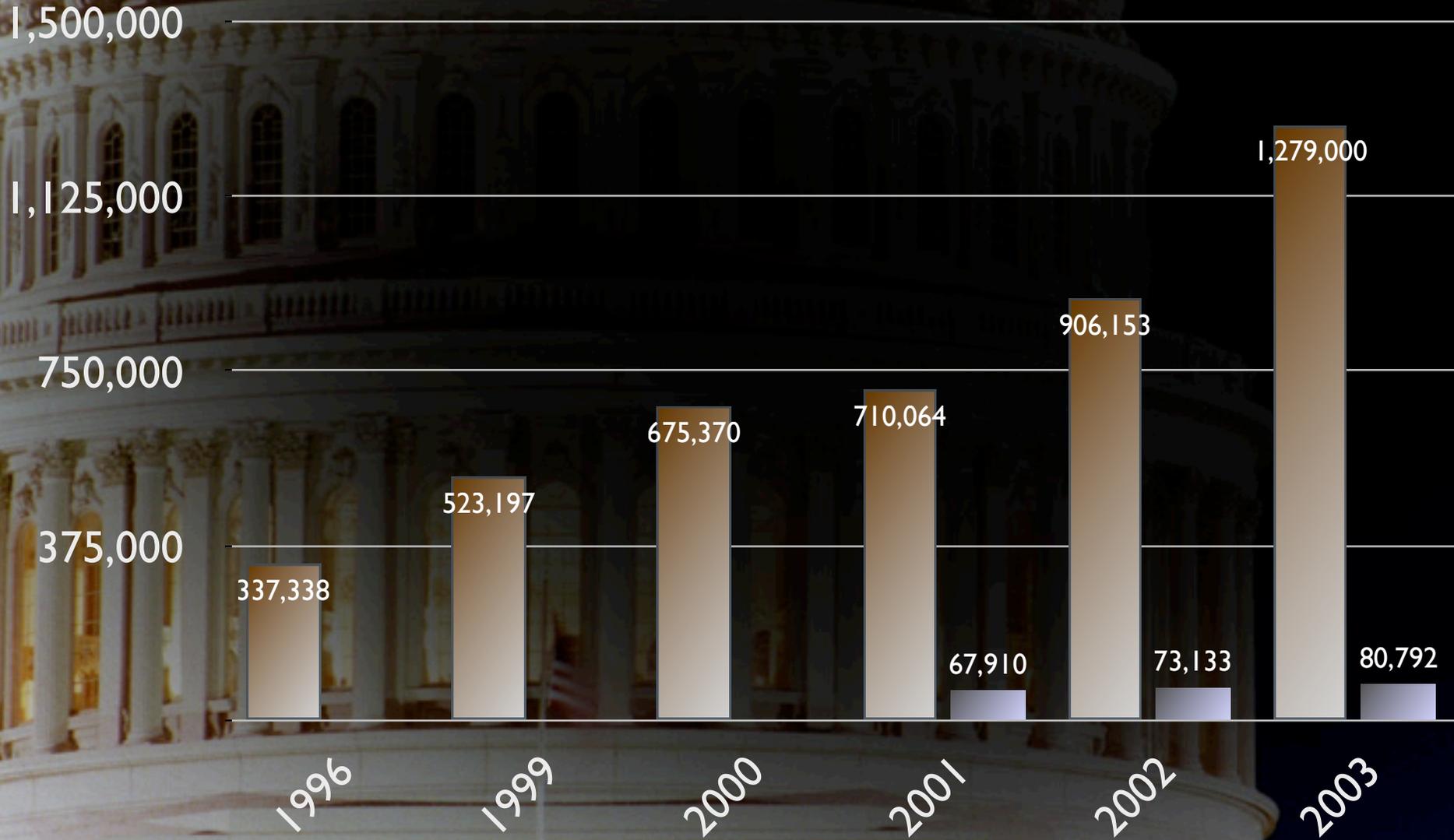
- (MS) musculoskeletal
 - ▶ includes ‘soft tissue’ grafts
- (OA) osteoarticular
- (DM) dura mater
- (C) cardiac
- (V) vascular
- (S) skin

But...realize we also cover:

- (R) reproductive
 - ▶ includes semen, oocyte, embryo
- (A) autologous
- (SB) living donor surgical bone
- (LD) living donors

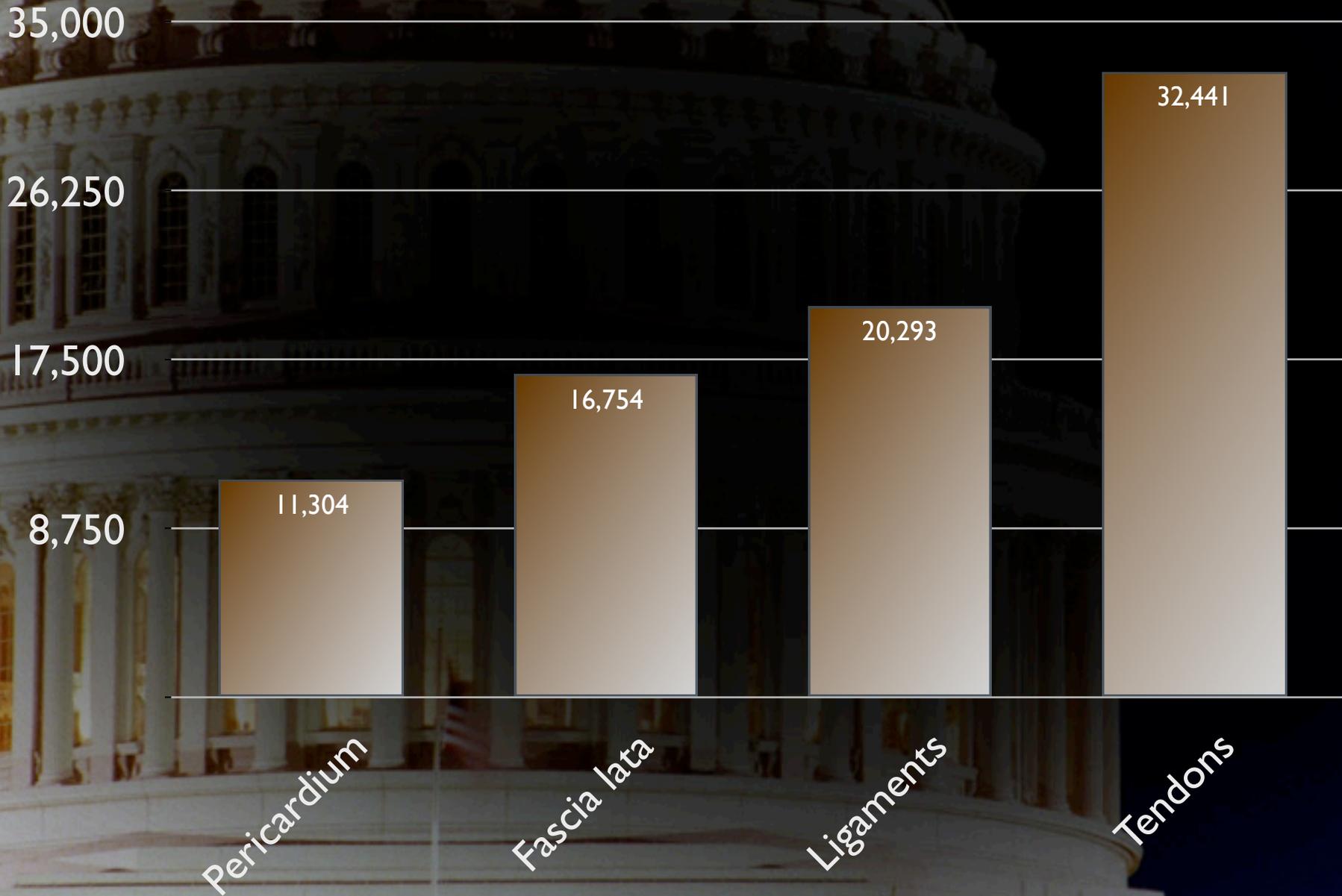
Musculoskeletal Allografts Distributed (includes bone & soft tissue)

■ Combined ■ Soft Tissue Only



AATB-accredited banks only

2003 Survey - Soft Tissue Distributed (80,792)



AATB-accredited banks only

MS Tissue Handling Flow

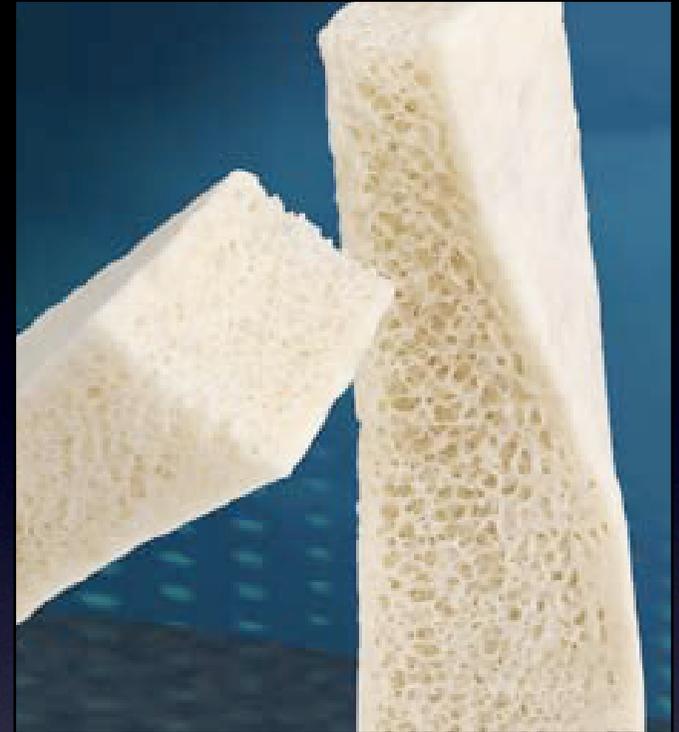
(includes soft tissues)

- Aseptic recovery (refrigerate or freeze)
 - ▶ Aseptic processing - clean, disinfect (refrigerate), or
 - ▶ Aseptic processing - thaw, then clean, disinfect (sterilize)
 - * non-terminal gamma irradiation (if indicated);
 - * chemical washes/soaks (alcohol, detergents, surfactants, hydrogen peroxide, etc.);
 - * agitation, sonication, centrifugation;
 - * possibly, demineralization (using acid - 0.5N HCL).
 - lyophilization (freezing, Residual Moisture content < 6%)
 - freezing or cryopreservation
 - ✓ terminal gamma irradiation (1.0 to 2.5 Mrads, 10 to 25 kGy)

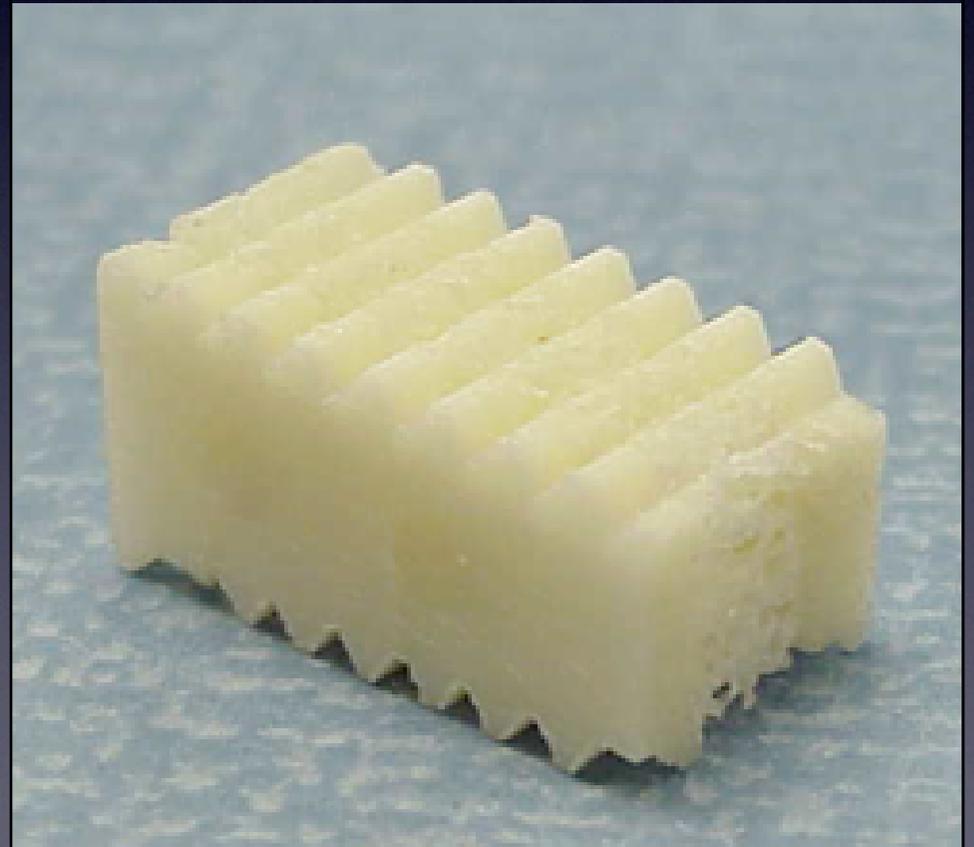
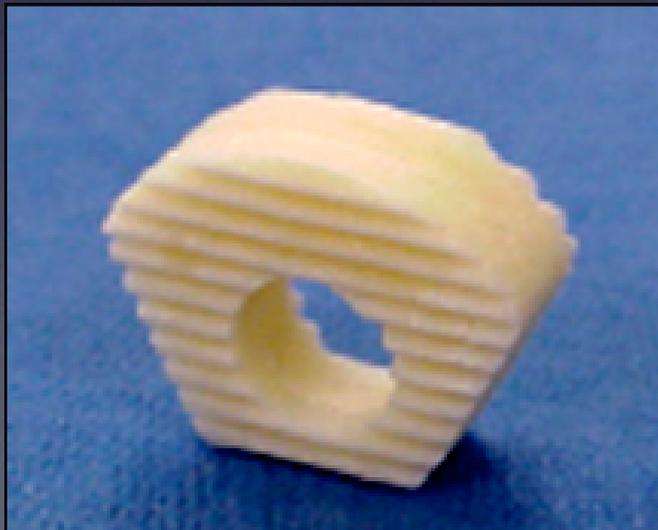
Demineralized & Lyophilized



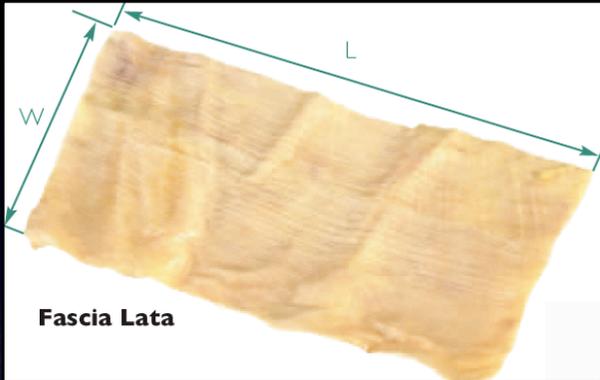
Lyophilized - "traditional"



Frozen - Tissue "Forms"



Fresh, Frozen, Cryopreserved, or Lyophilized (some can also be irradiated)



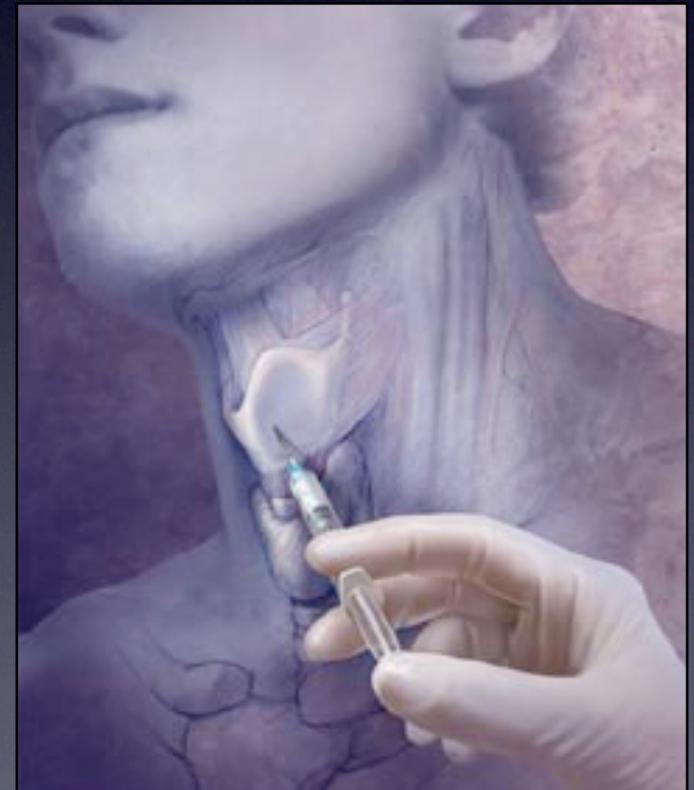
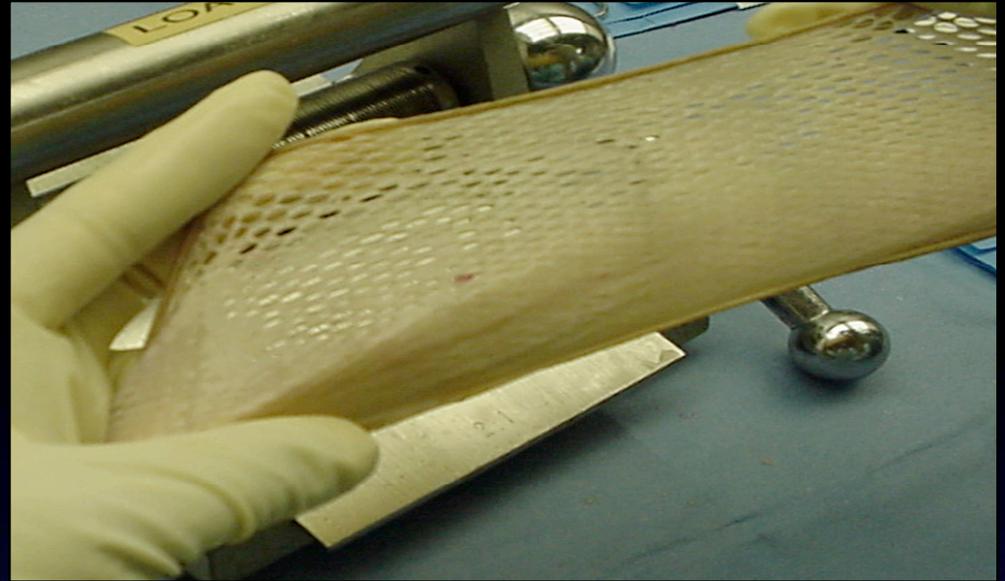
Fresh Osteochondral (osteoarticular) Joint

Knee
Ankle
Shoulder
Elbow



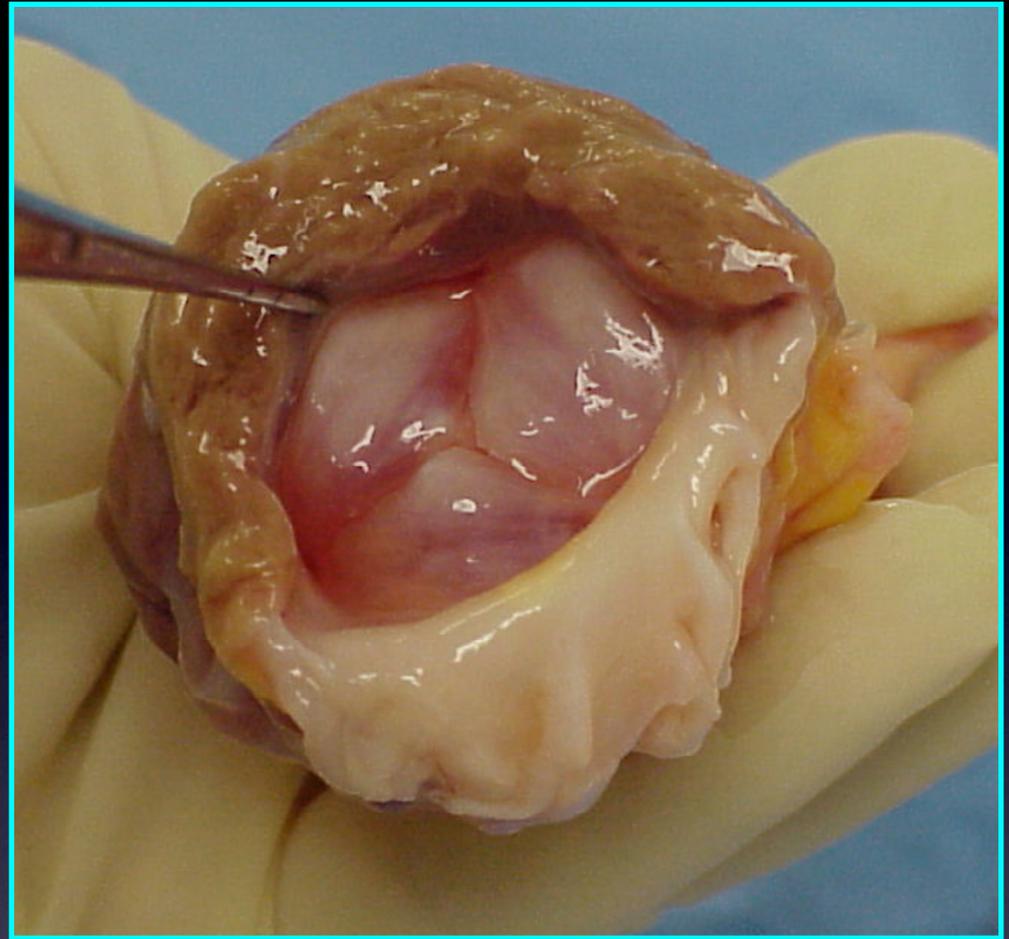
Skin

- Fresh
- Cryopreserved
- Lyophilized
- Decellularized, freeze-dried matrix
 - ▶ cryofractured - injectable



Cardiac & Vascular

- Disinfected w/ antibiotics
- Cryopreserved



Chagas Screening Since 2001

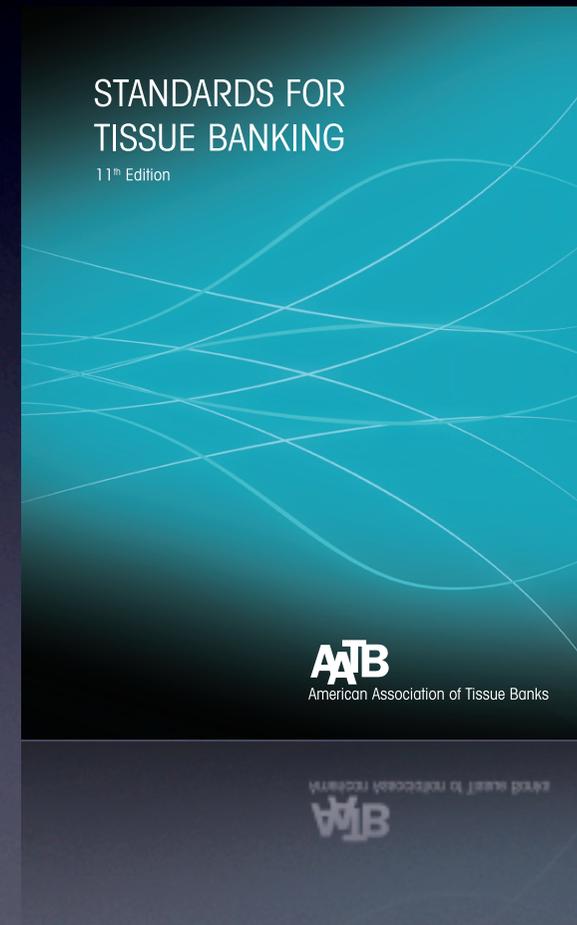
AATB *Standards* has required Chagas' disease screening for a specific tissue type (9th edition, 2001):

D4.000 Donor Suitability

(C) Heart donors shall also meet the following criteria:

.....

6) Heart valve donors shall be evaluated for the risk of Chagas' disease.



Rationale: *T. cruzi* has an affinity for myocardium and can be cryopreserved using current methods.

Preservation & Storage

- **Fresh** - refrigerated 1-10°C x 1 to ≈ 30 days
- **Frozen** - freezing **below -20°C** (short term < 6 months) or **long term below -40°C**
- **Lyophilized** - freeze-dried, kept at ambient temperature or colder up to 5 years
- **Cryopreserved** - freezing w/cryoprotectant; tissue type dependent:
 - ▶ storage temperature - either below -40°C or below -100°C
 - ▶ expiry - generally 2 to 5 years

Parasites

- Can be:
 - ▶ Preserved by refrigeration
 - ▶ Preserved by cryopreservation
 - ▶ Killed by simple deep freezing
 - ▶ Killed by lyophilization
 - ▶ Killed by irradiation
- Are not a risk for the majority of tissue grafts made available today



Courtesy of C. Ben Beard, PhD -
CDC

PROPOSED APPROACH TO REGULATION OF
CELLULAR AND TISSUE-BASED PRODUCTS

[Docket Number 97N-0068]

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Considerations

Tiered, risk-based approach, specifically in regard to 'conventional' HCT/Ps, when considering testing recommendations

▶ FDA's "Proposed Approach to Cellular and Tissue-based Products" (2-28-1997)

Considerations

- FDA could hold a public workshop with industry to become more aware of processing methods and validation procedures in use (in discussion)
- Donor screening test kits have **higher false-positive rates for cadaveric specimens** vs specimens from heart-beating donors
 - ▶ Current approved Chagas Ab test kit has significant false positive rate for living donors; labeling approval for cad specimens “inevitable”
 - ▶ RR donor screening test results = donor ineligibility determinations for HCT/Ps; **no chance for re-test**