General points of discussion

- Should we standardize techniques for the assessment of glucose metabolism?
  - What parameters can realistically and feasibly be standardized?
- Should we standardize presentation of techniques/results?
  - What information is absolutely required for interpretation of data?
- Should we make recommendations to the scientific community?
  - Is our charge to be educators (and “regulators”) or service providers?

If YES, how do we do this?

If NO, how can we increase transparency

Evaluation of Glucose Homeostasis

Contributed by Sami Heikkinen, Carmen A. Argmann, Marie-France Champy, and Johan Auwerx
Current Protocols in Molecular Biology (2007) 29B.3.1-29B.3.22

Table 29B.3.1 Summary of Methods Used to Assess Glucose Tolerance and Insulin Sensitivity[a]

Test	Labor intensity	Method	Interpretation
FPG and FPI	One blood sample (50–100 μl; tail bleed or retro-orbital)	Overnight or 4 hr fasting glucose and insulin measurements	Estimate of basal IR
HOMA	Simple calculations	Two formulas using FPG and FPI	Estimate of basal IR and β–cell function (not validated in mouse)
MTT	Two samples (50–100 μl; tail bleed or retro-orbital)	Overnight fast, and glucose and insulin measurements ± a standardized meal	Estimate of basal and postprandial IR; intestinal nutrient absorption taken into account
OGTT	Eight small samples (~3 μl) over 180 min (tail bleed)	Overnight fast, and glucose measurements after oral glucose load	Estimate of IR based on the evolution of glucose levels; intestinal glucose absorption taken into account
IPIST	Six small samples (~3 μl) over 90 min (tail bleed)	Overnight fast, and glucose measurements after IP insulin load	Estimate of basal insulin sensitivity based on the evolution of glucose levels
IPGTT	Eight small samples (~3 μl) over 180 min (tail bleed)	Overnight fast, and glucose measurements after IP glucose load	Estimate of IR based on the evolution of glucose levels
Euglycemic clamp	Catheter surgery, small blood samples every 5 to 10 min over 180 min (tail bleed)	Constant rate insulin infusion, variable rate glucose infusion; frequent glucose measurements	Estimate of IR based on average glucose infusion rate over the last 60 min; often regarded as the gold standard

[a]FPG, fasting plasma glucose; FPI, fasting plasma insulin; IR, insulin resistance; HOMA, homeostatic model assessment; MTT, meal tolerance test; OGTT, oral glucose tolerance test; IPIST, intraperitoneal insulin sensitivity test; IPGTT, intraperitoneal glucose tolerance test.

Clamps

Do we standardize clamp techniques?

NO

Recommendation:
Describe the protocol in detail

What parameters should be described?
- **Fast duration?**
- **Sampling site?**
- **Length of clamp?**
- **Tracer protocol?**
- **Mouse maintenance?**

YES

What parameters should be standardized?
- **Fast duration?**
- **Sampling site?**
- **Length of clamp?**
- **Tracer protocol?**

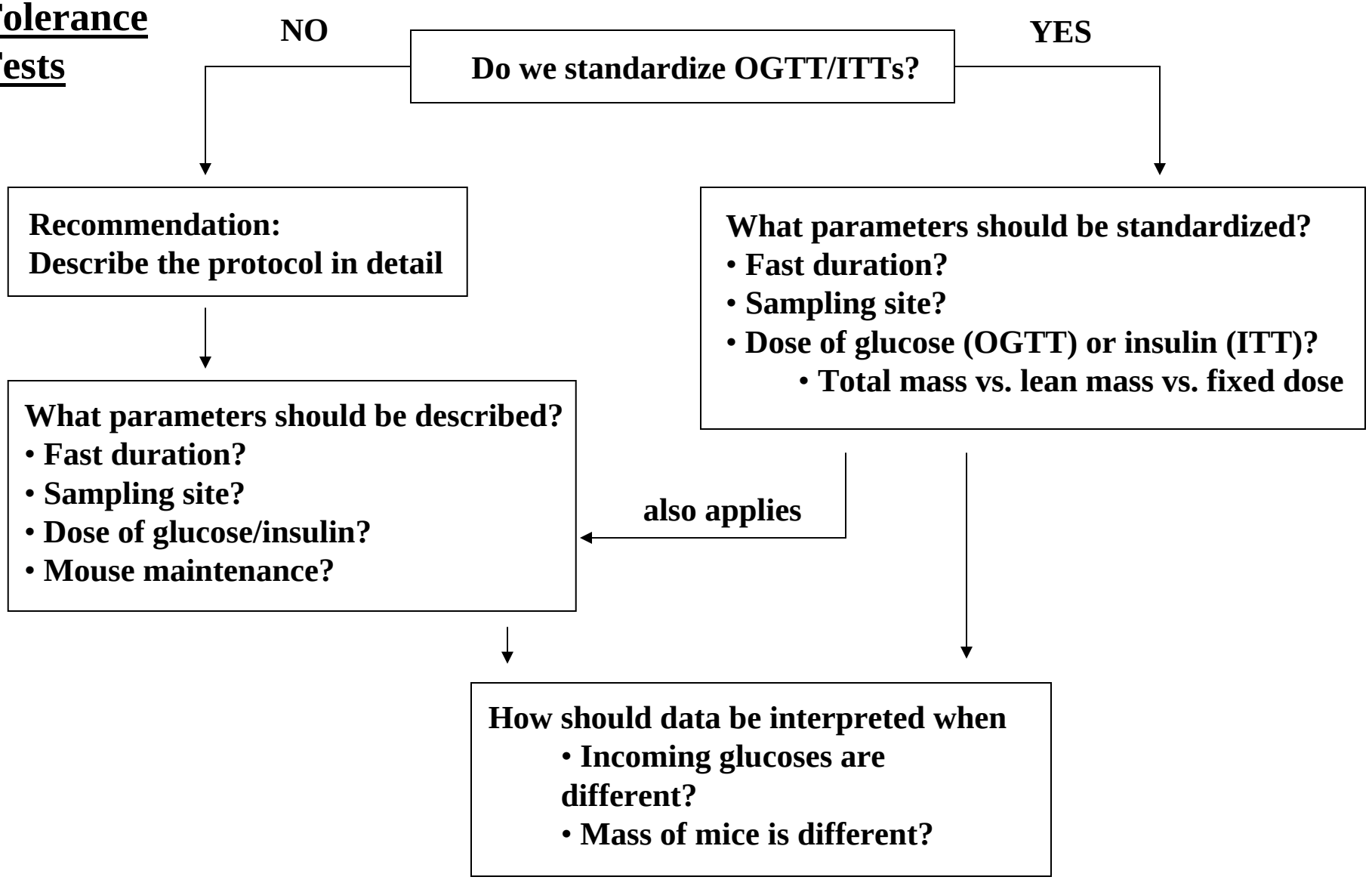
also applies

How should data be presented?
- **Time course plot vs. average data (bar graphs)?**
- **Absolute turnover or relative (e.g. % suppression of HGP)**

How should data be normalized?
- **Total vs. lean body mass? Insulin levels?**

What data should be presented?

Tolerance Tests



Other points of discussion:

- With regards to the clamp, do we (the MMPC Consortium) make recommendations on using a particular protocol?
  - If we do not agree on a standard protocol, do we provide information on bases for choosing one protocol over another?
- Do we make recommendations to users as to whether a clamp vs. a GTT/ITT is more appropriate for a question they are addressing?
  - i.e. do we act more as an “educator” rather than just providing a service
- Do we draft a manuscript comparing methods for assessing insulin action/glucose homeostasis?

- By what vehicle should recommendations/manuscripts be presented to the scientific community?
  - Journal? Website? Education courses?