

Community Opinions on the Collection and Use of Historical Control Data in Nonclinical Toxicity Studies

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Introduction

Access and use of historical control data was identified as a top concern of stakeholders across organizations according to results of a survey of needs and challenges related to nonclinical data conducted by the FDA/PhUSE Nonclinical Working Group in 2011. There is a perception that there may be additional ways to capitalize on historical control data to enhance studies or submissions across industry, academia, and government. During the working sessions of the FDA/PhUSE Computational Sciences Symposium in March 2012, a Historical Control subgroup of the FDA/PhUSE Nonclinical Working Group was formed to investigate how the industry might more effectively harness decades of data from untreated/vehicle control animals. The subgroup includes broad representation of stakeholders with interest in nonclinical data. Our poster describes our progress to date and includes results of a second survey to determine how organizations use and would like to use historical control data.

Survey Questions

Surveys were designed by the working group in collaboration with Instem and distributed via email (unrestricted) through personal and professional networks, including mailing lists for Instem, STP, relevant subsections of SOT, the Teratology Society, ACT, and the IQ consortium.

- Background: Organization Name & Type (CRO, Pharma, University, Government, etc.)
- Background: Respondent's Name, Email, primary role, and on whose behalf is the respondent answering the survey (self, department, facility, entire organization)
- Availability of historical control information to the respondent (2 Questions)
 - Do you currently use historical controls for the following types of data in your organization?
 - Does your organization maintain historical control data for other data types not listed above?
- Respondent's use of historical control data (2 Questions)
 - For a variety of scientific activities, agree or disagree with the following: "Having historical controls data is or would be useful for me for the following activities"
 - If applicable, please list and describe any other uses of historical control data that are not listed above.
- What limits the respondent's use of historical control data? (responses include a list of suggestions and "other")
- What projects involving historical control data do you think would be a useful undertaking for the nonclinical community? (responses include four suggested projects and "other")
- General information related to historical control data (6 Questions)
 - What methods are used to summarize/analyze your historical control data (manual; automated – vendor system; automated – internal system; other)?
 - Are any of the systems that you use to summarize/analyze historical control data validated for GLP compliance?
 - What percent of your studies use tabulated historical control data for interpretation and/or reporting?
 - Would your organization be willing to share its historical control data with other organizations?
 - Would your organization like to increase use and access to historical control data?
 - Any final comments?

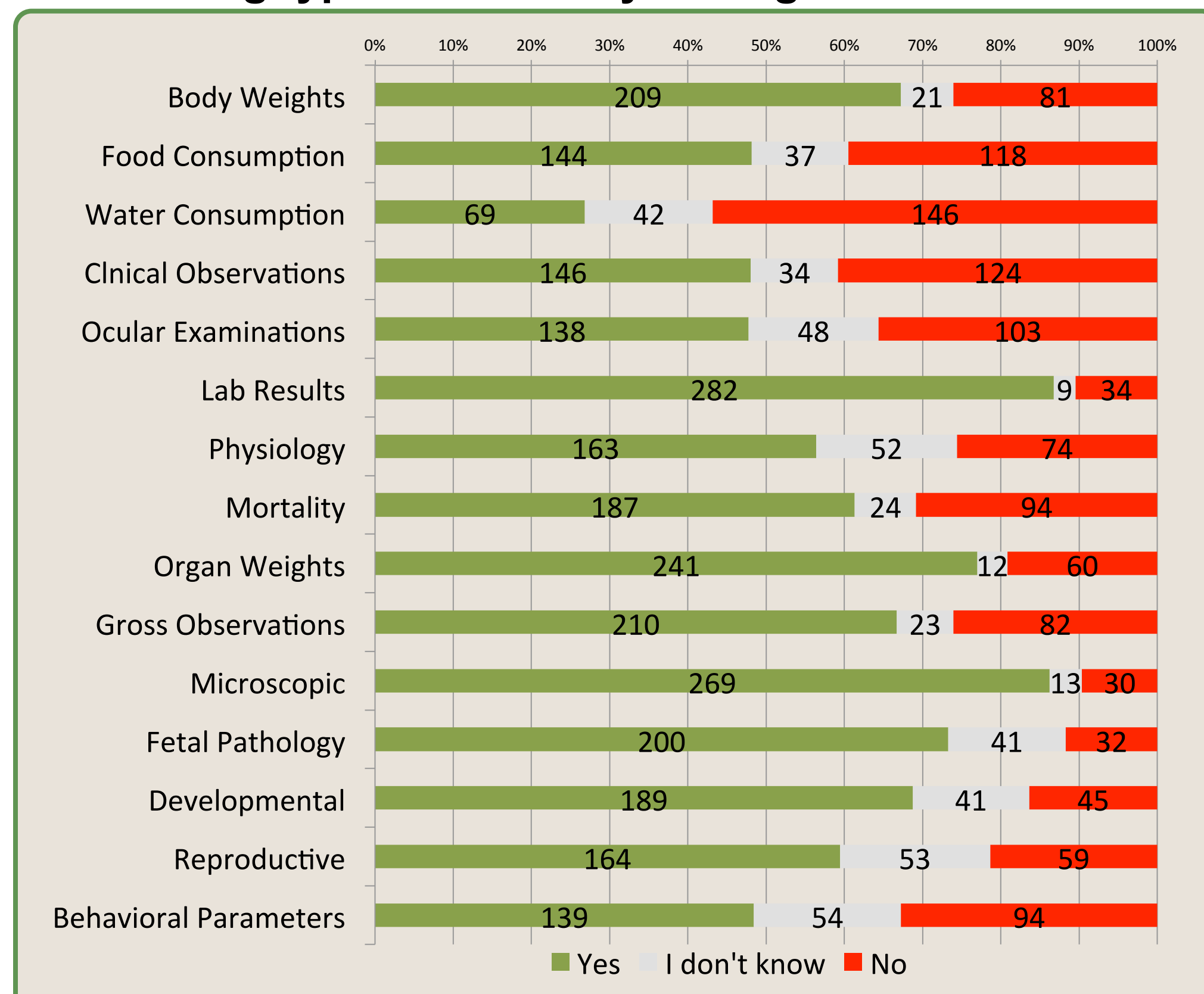
Survey Example

Do you currently use historical controls for the following types of data in your organization? Use 'Not Applicable' if this type of data is not collected in your organization.

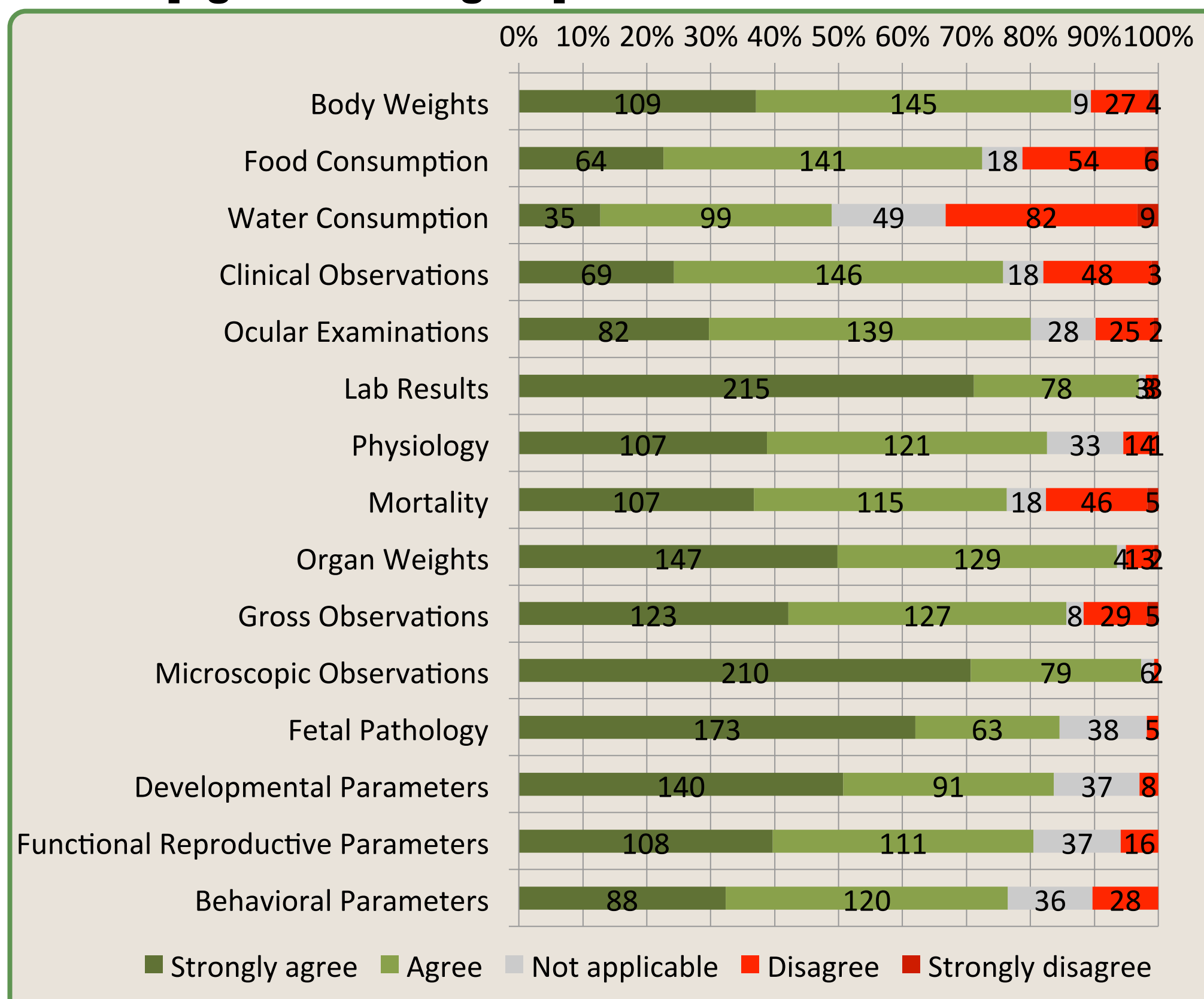
	Yes	No	I don't know	Not applicable	Rate this statement: Having historical control data for this data type is or would be useful to my organization
Body Weights and Weight Gains	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
Food Consumption	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	Strongly agree Agree Disagree Strongly disagree Not applicable
Water Consumption	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
In-Life Observations (clinical signs, veterinary observation...)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
Ocular Examination Data	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
Laboratory Results (Hematology, Serum Chemistry, Urinalysis...)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
Physiological Data (Cardiovascular, CNS, Respiratory Evaluations...)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
Mortality	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
Organ Weight Parameters	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
Gross Pathology Findings	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
Microscopic Findings (non-neoplastic or neoplastic)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
Fetal Pathology Findings (malformations, variations...)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
Developmental Parameters (survival, body weight, milestones)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
Functional Reproductive Parameters (estrus cycle / semen analysis)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --
Behavior parameters (FOB, Motor Activity...)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	-- Please Select --

Results

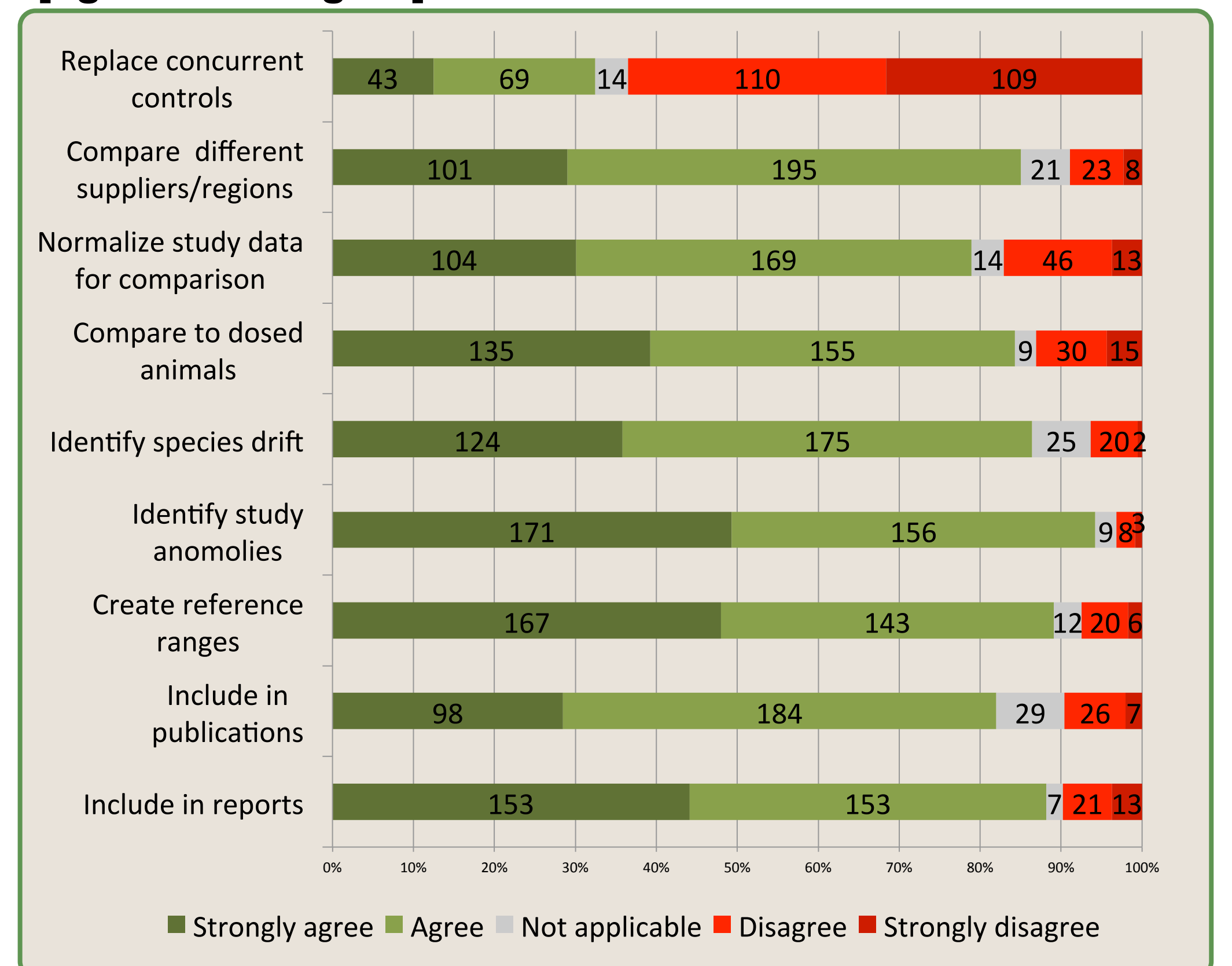
Do you currently use historical controls for the following types of data in your organization?



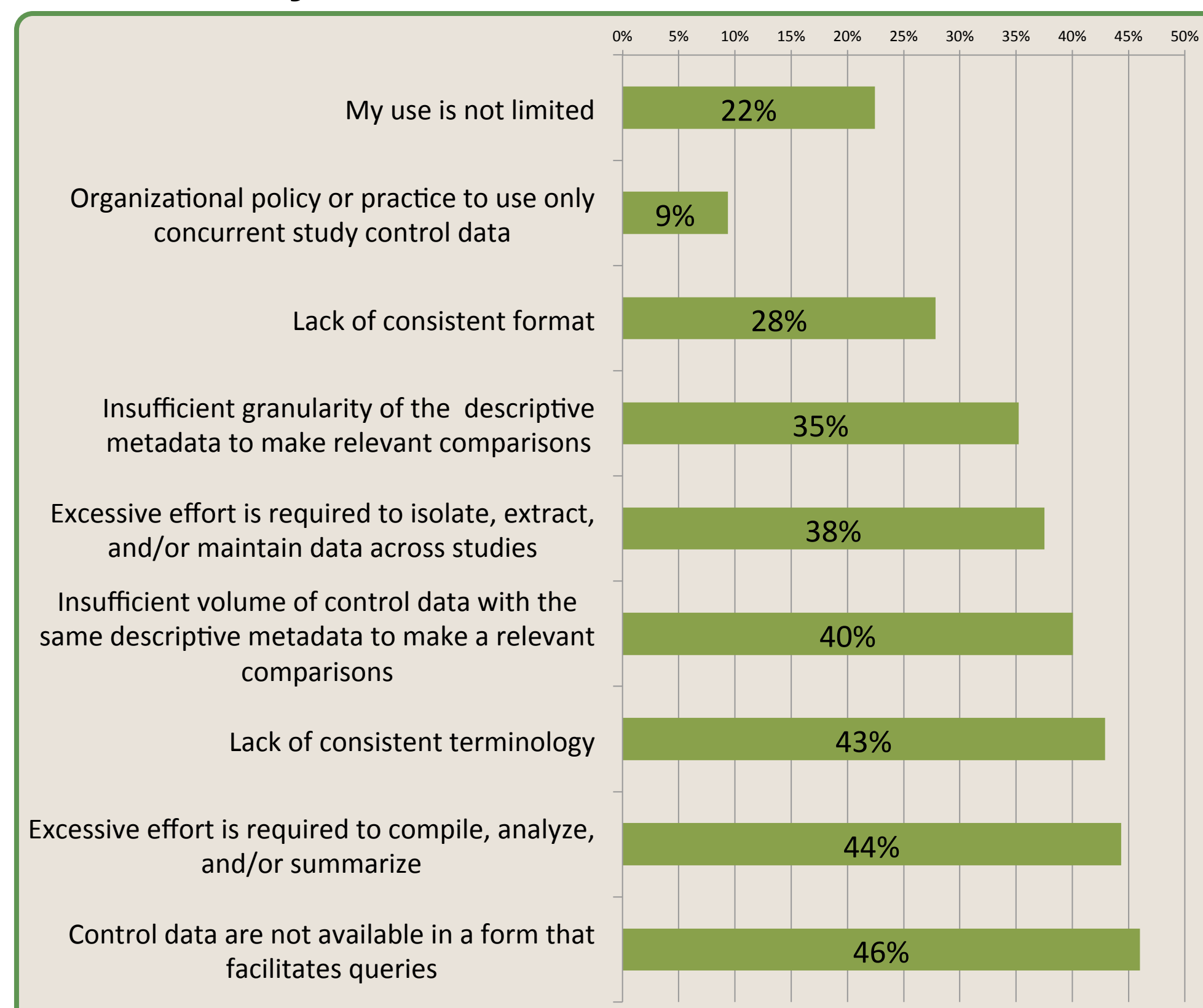
Historical controls for the following types of data are useful [agree or disagree]:



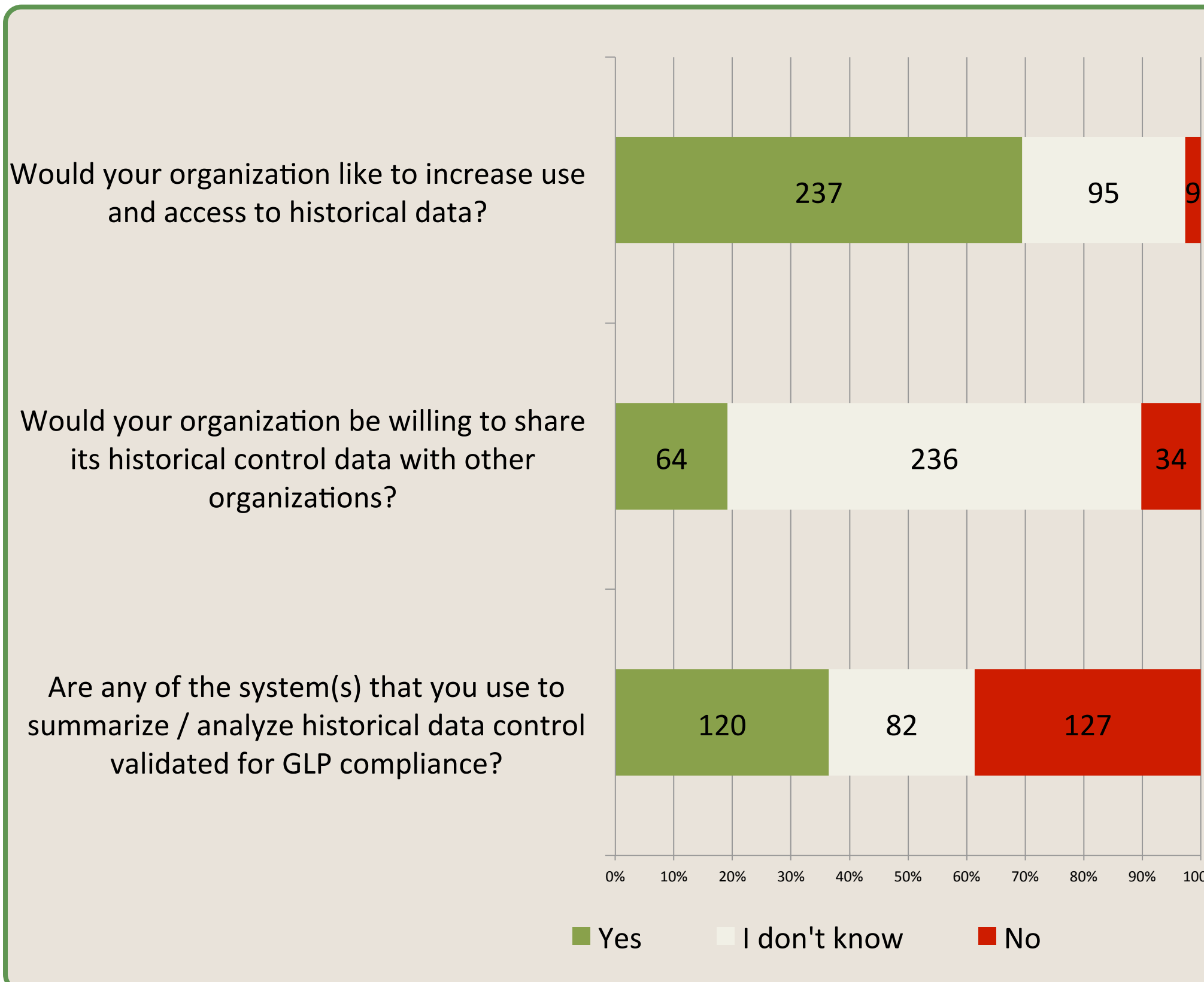
Historical controls data is useful for these activities [agree or disagree]:



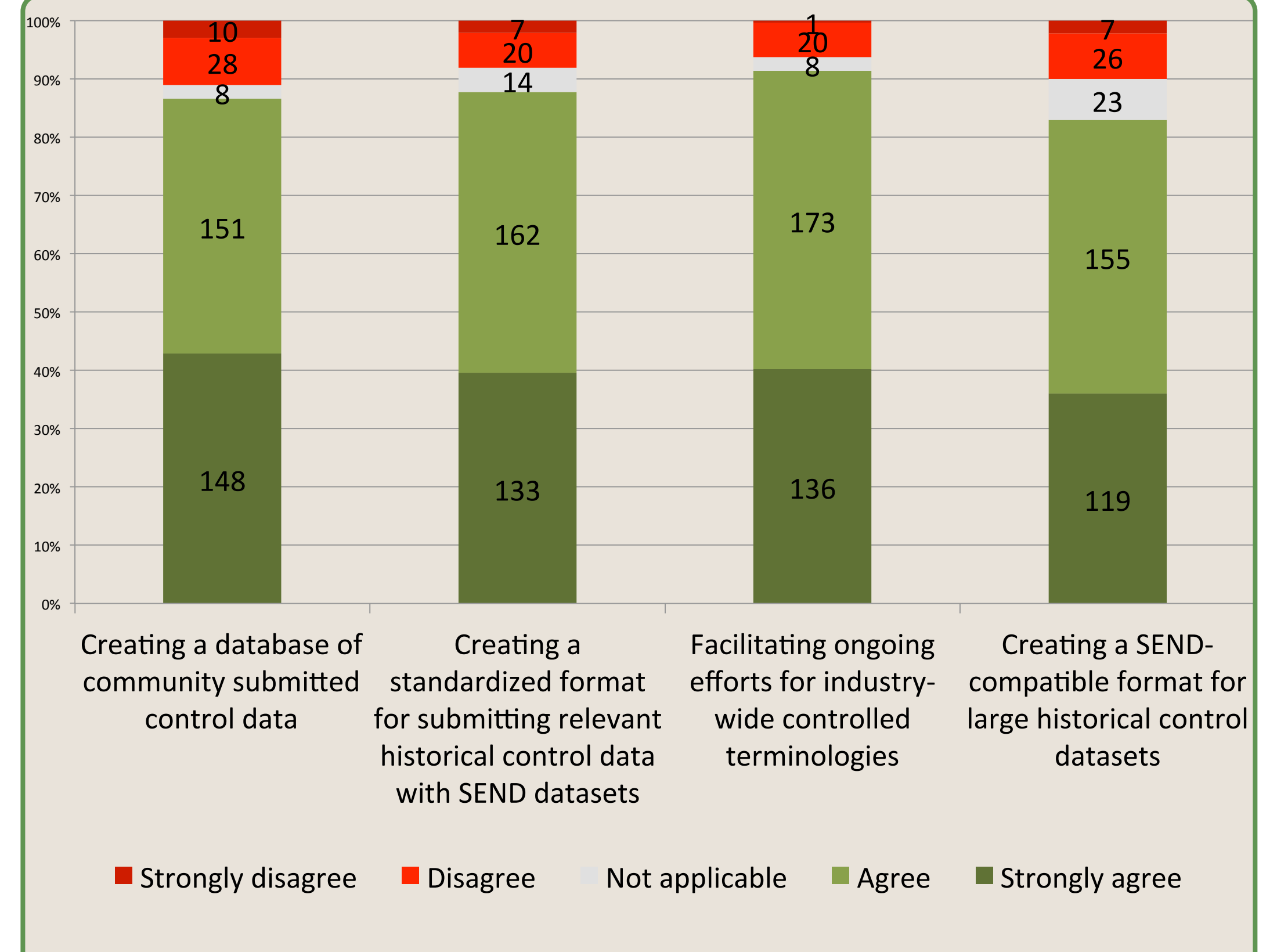
What limits your use of historical control data?



Other questions



What projects involving historical control data do you think would be a useful undertaking for the nonclinical community?



Survey Respondents

- 352 respondents completed the survey, mostly from North America (73%). They were from pharmaceutical companies (40%), CROs (31%), consultancies (13%), government (6%), and other (6%)
- 70% reported answering for themselves versus 35% for their department/facility/organization.
- Respondents described themselves as pathologists (27%), management (16%), consultants (11%), study directors (10%), study monitors (10%), development team members (8%), reviewers (3%), researchers (3%), regulatory affairs (3%), or operations (3%).

Conclusions

- The nonclinical community is interested in increasing its use of historical control data.
- HC data for clinical pathology and post-mortem findings types are perceived as more valuable than others.
- Replacing concurrent controls with HC data was not widely supported.
- Many factors currently limit HC data use.
- Relevant stakeholders expressed enthusiasm for most of the suggested projects.

NOTE: The opinions expressed in this poster are those of the authors and do not necessarily represent the opinions of their representative organizations.