BEYOND INFORMED CONSENT: FACILITATING INNOVATION IN A JUST WORLD

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INFORMED CONSENT PARADIGM FOR RESEARCH ETHICS

- Informed by experience with Nazi Experimentation on Human Beings
- Exploitation of vulnerable subjects
- Human Beings as mere instruments
  - No consent
  - No concern for subjects' interests or safety
  - No benefits
  - Non-medical over medical purposes

CONTINUING RELEVANCE OF INFORMED CONSENT

- Uneven relationship between investigator and research
- Risks inherent to experimentation
- Injustices abound
  - Use of subjects who can never benefit from findings
  - Excessive recruitment of the economically challenged
  - Inequitable access to benefits

CONTINUING RELEVANCE OF INFORMED CONSENT

- In international research, subjects' distance from conceptualizers of research is magnified.
  - Lack opportunity for timely and weighty feedback
  - Inadequate understanding of research
  - Failure to appreciate subjects' interests

HOW PATIENTS (COULD?) BECOME SUBJECTS

- Having tissues/samples taken for diagnostic examination
- Participating in non-genetic research that requires tissues to be drawn and stored
- Submitting oneself for genetic testing
- Undergoing In Vitro Fertilization
- Having a genetic relative participate in research in any of the above ways

HOW PATIENTS (COULD?) BECOME SUBJECTS

- Having one's records kept in a hospital
- Being the recipients of aid after a disaster
- Being a patient in an emergency situation

ISSUES WITH PREVAILING INFORMED CONSENT PARADIGM

- Ethical requirements of consent for all future uses cannot be satisfied at the time a potential research subject is engaged.
- Tissue Providers (TPs) have generally expressed willingness to contribute to research with only minimal information about a study
- Puts a great deal of responsibility on the TP
  - To make a decision at the outset
  - To give up control over donated material at the time consent is taken

Studies about Informed Consent

Study in Vasterbotten, Sweden:

- Hoeyer et al:
  - Informed consent and biobanks: a population-based study of attitudes towards tissue donation for genetic research

- General acceptance of genetic research based on biobank material (71%)
- Majority (62%) would not allow researchers to examine their healthcare records without specific consent.

Study in Vasterbotten, Sweden:

- Majority (66.8%) accepted surrogate decisions by research ethical committees;
- 48% would feel respected if they were notified each time a sample was used.
- Re future health risks, a majority (55%) would want to be told only if treatment was available
- Informed consent was a principal concern to a minority (4%) only.

Consent to use of Residual Tissue among Cancer Patients in the Netherlands

- Vermeulen et al:
  "Obtaining 'fresh' consent for genetic research with biological samples archived 10 years ago"

- One-time general consent' was considered to be the best procedure for consenting to research with stored tissue by 56%,
- 23% favoured the current 'opt-out' procedure;
- 21% did not know or had no preference.

Willingness to donate blood samples for genetic research: community sampling

- 49.3% (95% CI, 45.1–53.5%) were willing to donate blood for genetic research
- willingness was significantly associated with:
  - belief in the benefits
  - intention to participate in government studies;
  - having no fear of pain, blood, injections, and needles; and
  - non-concern about the loss of confidentiality

Wong, et al. Clinical Genetics, Volume 65, Number 1, January 2004 , pp. 45-51(7)

Wendler Metadata: One-time General Consent

- (79-95%) willing to provide one-time general consent and rely on ethics committees to determine the studies for which their samples would be used.
- Even research on potentially stigmatising conditions

David Wendler BMJ 2006;332:544-547

Wendler Metadata: One-time General Consent

- Three studies: people marginally less willing to provide a sample for commercial rather than academic research.
- Nine studies: like some information on the projects for which their samples will be used, although the type of information desired was not specified.

David Wendler BMJ 2006;332:544-547

Wendler Metadata: One-time General Consent

- Ethics committees to determine that future projects are acceptable and pose no more than minimal risks
- Increases scientific and social value of donated samples
- Lowers costs of conducting research by eliminating the need to track the choices for each sample.
- Minimizes inconvenience of being repeatedly contacted and asked for consent

Matsui, "The Ethics of Non-Specific Consent to Unforeseen Uses of Biobanked Materials: Donors' Views and Rationales" (2012)

Table 3. Consent rates to the sharing of donated samples/data

Consent items	All donors (N = 336)	Male (N = 138)	Female (N = 198)
	Number (%)	Number (%)	Number (%)
Allowing my data to be provided to the *Tougoukenkyu* of the JALS[a]	322 (95.8)	132 (95.7)	190 (96.0)
Allowing my samples/data to be provided to the J-MICC Study[b]	162 (95.3)	55 (96.5)	107 (94.7)
Allowing my samples/data to be provided to various unspecified future (collaborative) research	291 (86.6)	122 (88.4)	169 (85.4)

Abbreviations: JALS, Japan Arteriosclerosis Longitudinal Study; J-MICC Study, Japan Multi-Institutional Collaborative Cohort Study.

Matsui, "The Ethics of Non-Specific Consent to Unforeseen Uses of Biobanked Materials: Donors' Views and Rationales" (2012)

Re-consent conditions	All consenters to unspecified future research (n = 289)[a]	Male (n = 120)[a]	Female (n = 169)
	Number (%)	Number (%)	Number (%)
No need to re-obtain my (or my family's) consent at a new research proposal provided that the institutional research ethics committee approves it	223 (77.2)	92 (76.7)	131 (77.5)
Need to re-obtain my (or my family's) consent at every new research proposal in addition to the approval by the institutional research ethics committee	64 (22.1)	28 (23.3)	36 (21.3)
N/A	2 (0.7)	0 (0.0)	2 (1.2)

[a] Two male subjects who chose both conditions at the same time were excluded.

DELIBERATIVE APPROACH

- Secko et al:
  Informed consent in biobank research: a deliberative approach to the debate

- Strong support for biobanks
- General reduction in concern for withdrawal of samples
- Need for review of biobanks research that is independent of funders and researchers.
- Persistent disagreement about when consent was required for new research activities

Can open consent be 'informed'

- Hallinan & Friedewald:
  Open consent, biobanking and data protection law: can open consent be 'informed' under the forthcoming data protection regulation? 2014

- Open consent cannot meet information requirements with adequate specificity:
  - Purpose,
  - Recipient,
  - Possible third country transfers,
  - Data collected
- Applicable consent requirements should be rethought

Can open consent be 'informed'

- Hallinan & Friedewald:
  Open consent, biobanking and data protection law: can open consent be 'informed' under the forthcoming data protection regulation? 2014

- Open consent in biobanking does not present great risk to subject
- There are grounds for a reconsideration of consent requirements
- Provide legal protection against the harms that could come through the use of data by third parties
- Protection can be provided outside the research process

Informed Consent and Comprehension

- Beskow et al:
  Informed consent for biobanking: consensus-based guidelines for adequate comprehension

- Consensus (>70% agreement) concerning what specific details participants should know about 16 biobank consent topics.
- Achieved for 15 of the 16 consent topics.
- Exception: comprehension needed regarding the Genetic Information Nondiscrimination Act

Informed Consent and Comprehension: Recommendations

- Beskow et al:
  Informed consent for biobanking: consensus-based guidelines for adequate comprehension

Improve consent forms:

Focus on information most important to prospective participants.

Informed Consent and Comprehension: Recommendations

- Beskow et al:
  Informed consent for biobanking: consensus-based guidelines for adequate comprehension

Improve consent processes:

Focus on effectively communicating the most crucial information

Informed Consent and Comprehension: Recommendations

- Beskow et al:
  Informed consent for biobanking: consensus-based guidelines for adequate comprehension

Facilitate research on biobanking consent

Consent form topic	Adequate comprehension?[a] *n* (%)		
		Disagree[b]	
	Agree	Too little	Too much
Biobank purpose: "The purpose of this project is to collect and store samples and health information for use in future research."	41 (87)[c]	6 (13)	0 (0)
Blood draw: "You are going to draw blood from me."	35 (74)[c]	12 (26)	0 (0)
Collection of information: "You will ask me some basic information and will contact me to update this information. You will also collect information from my medical records."	46 (98)[c]	1 (2)	0 (0)
Duration of storage: "My sample and information will be stored forever unless I decide to stop taking part."	46 (98)[c]	0 (0)	1 (2)
Access to biospecimens/data: "Researchers may study my samples and information. You will not give researchers information that could identify me."	35 (74)[c]	11 (23)	1 (2)
Recontact: "Someone from the biobank may contact me about participating in additional research."	41 (87)[c]	5 (11)	1 (2)
Large-scale data sharing: "Some of my information might be put into a database. There is a small chance that someone could trace my information back to me."	39 (83)[c]	5 (11)	3 (6)
Risks: "There is a risk that someone could get access to information about me."	33 (70)[c]	11 (23)	3 (6)
Confidentiality protections: "You will take many steps to protect my privacy."	43 (91)[c]	2 (4)	2 (4)
Genetic Information Nondiscrimination Act: "There is a law against discrimination based on my information."	28 (60)	12 (26)	7 (15)
Alternate: There is nothing in this section a prospective participant must understand to give valid consent.	25 (53)	NA	NA
Certificate of confidentiality: There is nothing in this section a prospective participant must understand to give valid consent.	36 (77)[c]	NA	NA
Potential benefits: "I should not expect to benefit from this research."	45 (96)[c]	1 (2)	1 (2)
Costs and payments (commercialization): "I will not get money from anything that is done using my sample."	43 (91)[c]	3 (6)	0 (0)
Return of results: "I should not expect to get individual results back from this research."	40 (85)[c]	6 (13)	0 (0)
Discontinuing participation: "I have the right to leave the project. However, I cannot withdraw or get back samples and information from studies that have already begun."	41 (87)[c]	2 (4)	4 (9)
Questions or problems: "There is someone I can contact if I have questions or want more information."	46 (98)[c]	0 (0)	0 (0)

[a]Agreed or strongly agreed on a four-point scale in response to "How much do you agree or disagree that the statement above generally represents adequate comprehension of the consent topic?" [b]Among those who disagreed or strongly disagreed that the statement represents adequate comprehension, responses to question about whether the statement reflects more or less than a prospective participant needs to understand to provide valid consent. [c]Reached consensus, predefined as >70% agreement

CONSENT FORM TOPICS

DONATION AS AN OPTION

- Views of subject donors regarding donation of samples: 85.3 – 98.5% (England, France, India, Japan, Singapore, Sweden, Uganda, UK & US)
- Positive Views of public non-donors:
  - De Costa, 2004: 59 Indians – 86%
  - Wong, 2004: 708 Singaporeans – 49.3%
  - Ashcroft, 2003: 155 UK – 100%
  - Schwartz, 2001: 1383 Jewish Americans - >80%
  - Wang, 2001: 3130 US – 79%
  - Mertz, 1996: 99 US – 60%

Prevailing Consent Paradigm:

- Fails to reflect preferences of research participants
- Puts unnecessarily heavy burden on participants to protect their interests
- Indicates a need for governance model adapted to variable research conditions and information requirements.

DYNAMIC CONSENT

- Informed about broad range and foreseeable details of potential uses
- Withdrawal of consent at any time for any reason (or even no reason) without adverse repercussions
- Potential donors' option of not having to reconsent in future if they so choose

Dynamic Consent

- Subject-stipulated exceptions and options
- Clear protocol for withdrawal
  - Reasonable deadline
  - Clarity about what happens to information after withdrawal

DYNAMIC CONSENT

- Allows for individuals to be informed about or counseled on what is at stake, up to the level at which they feel their autonomy has been respected

Dynamic Consent: Option to Keep Informed

- Accepts the need to update the list of potential uses periodically, seeks to inform donors of the updated list
- Mechanism for donors to keep informed about developments with respect to research materials if they want to
- Accessible website or regular newsletters that contributors can either read or ignore

Dynamic Consent

- Co-guardianship of the donated samples with a research ethics board or an oversight body on specific uses of the donated material.
- Ethics Committee approval for each use
- Continuing Ethics Committee Oversight

Institutional Accountability

- Accreditation of research institutions
- Institutionally based Researchers and ECs
- Requirement for local institutional affiliation of researchers

Legal Framework

- Export and import of materials
- Materials Transfer Agreements
- Local institutional participation in foreign-sponsored research

Transparency

- Registration/ Publication of research and research outcomes
- Availability of updated information on use of HBMs

More Recommendations

- Involve civil society representatives in ethics review
- Public consultation regarding population genetics research
- Raise general public's level of awareness

TIME TO SHIFT FOCUS?

FROM CLOSED CONSENT

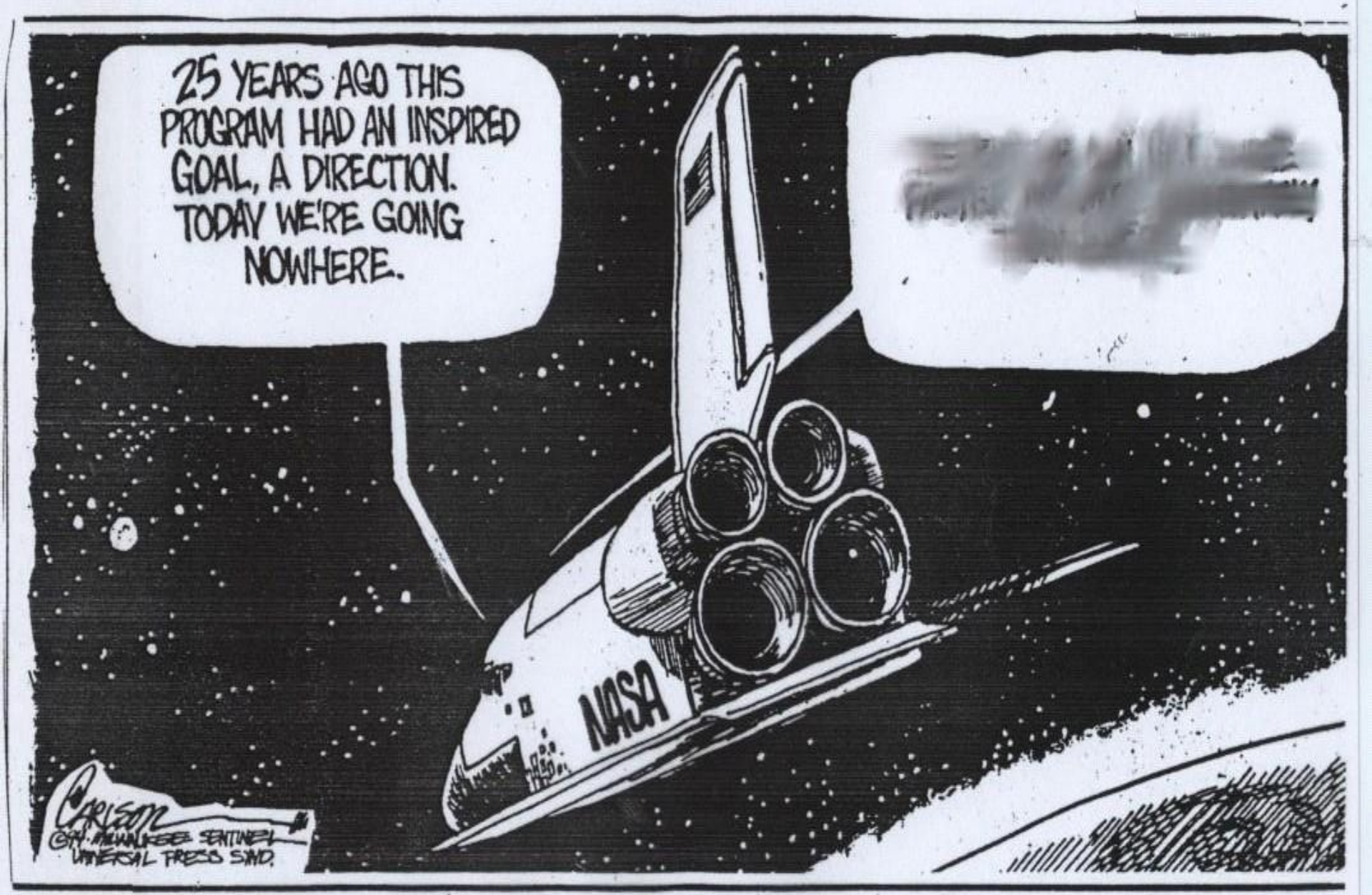
TO DYNAMIC CONSENT

INNOVATION: FREEDOM OF RESEARCH

- FREEDOM OF THOUGHT
- RESPONSIBILITY TO EXPLORE HUMAN POTENTIAL
- RESPONSIBILITY OF ALL HUMAN BEINGS

INNOVATION FOR WHAT?

- WHERE ARE WE GOING?
  - A sense of where we are
  - A sense of where we want to be
  - A SENSE OF PURPOSE


25 YEARS AGO THIS PROGRAM HAD AN INSPIRED GOAL, A DIRECTION. TODAY WE'RE GOING NOWHERE..
[redacted]
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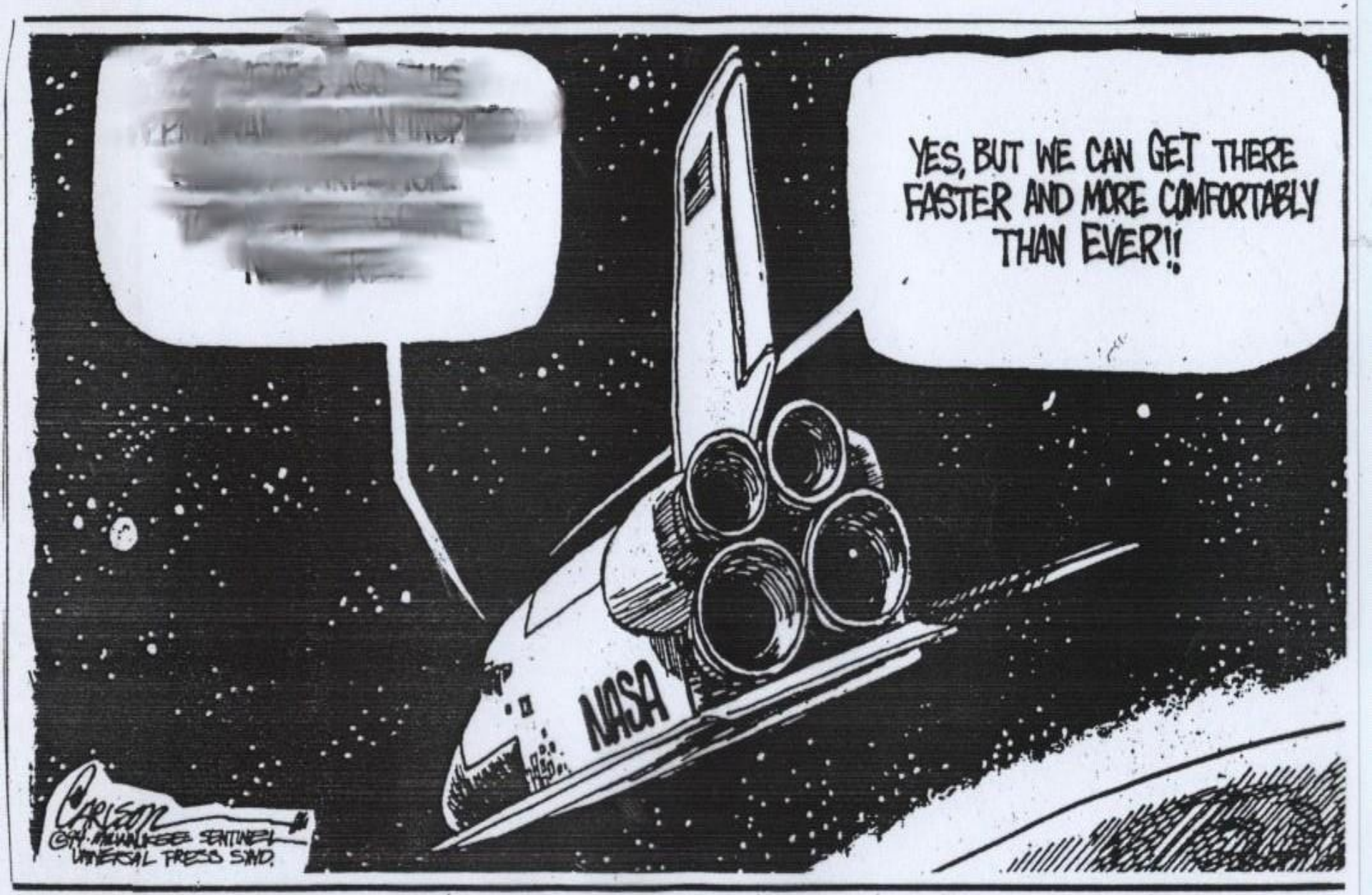
YES, BUT WE CAN GET THERE FASTER AND MORE COMFORTABLY THAN EVER!!
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INNOVATION FOR WHOM?

- Relevance to the weak and vulnerable
- Access to benefits by the research population
- Access to benefits by the poor and vulnerable

INNOVATIVE RESEARCH

INNOVATIVE ETHICS REVIEW

A SHIFT OF FOCUS

FROM ETHICS (P)REVIEW

TO ETHICS OVERSIGHT

DYNAMIC CONSENT