THE RAC: TO BE OR NOT TO BE

- RECOMBINANT DNA ADVISORY COMMITTEE (RAC)
- NIH REQUESTS INSTITUTE OF MEDICINE (IOM) RAC REVIEW
- IOM REPORT ON THE FUTURE ROLE OF RAC REVIEW
- RAC REVIEW OF VORINOSTAT + AGS-004
- COMMUNITY RAC ACTION
- THE FATE OF VORINISTAT + AGS-004
THE RAC: TO BE OR NOT TO BE

- **THE RAC: INSTITUTED IN 1974**
  - OVERSIGHT OVER NEW RECOMBINANT DNA TECHNOLOGY
  - TRANSFER OF GENETIC MATERIALS INTO HUMANS
  - TO REPLACE OR COMPENSATE FOR ABNORMAL GENES
  - TO ENHANCE IMMUNE SYSTEM TO FIGHT CANCER
  - FRANCIS COLLINS REQUESTED IOM RAC REVIEW-2013
THE RAC: TO BE OR NOT TO BE

RAC REVIEW QUESTIONS

- Does human gene transfer research raise special issues that warrant continuing extra oversight?

- Same level of concern is not present today after hundreds of clinical trials have evaluated safety and effectiveness.

- IOM report concludes that RAC oversight is arguably overlapping and redundant in light of FDA and IRB review.
THE RAC: TO BE OR NOT TO BE

- DIRECTOR COLLINS REQUIRES CONDITIONS FOR RAC REVIEW- 2014:
  - REVIEW CANNOT BE ADEQUATELY CONDUCTED BY FDA, IRBS, ETC.
  AND
- ONE OR MORE OF THE FOLLOWING CRITERIA ARE PRESENT:
  - NEW VECTOR, GENETIC MATERIAL OR FIRST-IN-HUMAN DELIVERY METHOD
  - PRECLINICAL SAFETY DATA OBTAINED USING NEW UNKNOWN AND UNCONFIRMED PRECLINICAL MODEL SYSTEM
  - POSSIBLE TOXICITIES THAT ARE NOT WIDELY KNOWN
THE RAC: TO BE OR NOT TO BE

- **RAC REVIEW vs A RAC PUBLIC HEARING**
  - Expedited review can be conducted quickly without the need for a public hearing.
  - Public hearing requires approximately four extra months based on quarterly RAC meeting schedule.
THE RAC: TO BE OR NOT TO BE

- Vorinostat + AGS-004 (David Margolis & Cynthia Gay, UNC)
  - Phase I study measuring the potential AGS-004 + Vorinostat (VOR)
  - Will a combination of serial AGS-004 vaccinations and VOR result in a depletion of persistent, latent HIV infection?
  - N= 12 HIV+ men/women, ≥ 18, on stable cART, suppressed for ≥ 2 years with CD4s ≥ 300, followed up to 96 weeks
  - Patients with measurable increases in HIV RNA expression frequency in CD4+ cells exposed ex vivo to VOR will proceed to the active phase of the study and will receive multiple doses of VOR + AGS-004.
THE RAC: TO BE OR NOT TO BE

- RAC REQUIRED PUBLIC HEARING
- OCCASIONED A FOUR MONTH DELAY
- PATIENT ENROLLMENT MILESTONE WAS MISSED
- FUNDING DELAYS RESULTED
- NEW COLLINS CONDITIONS FOR REVIEW NOT PRESENT
- NO GENE MODIFICATION PRESENT
- UNNECESSARY DELAYS SLOW RESEARCH
- ADVERSELY AFFECTS PEOPLE WITH HIV
THE RAC: TO BE OR NOT TO BE

- Community Action
  - Testimony at RAC Hearing
  - MDC CAB Letter to RAC Exec Secretary Lyric Jorgenson
    - Collins Criteria Be Required For Public Hearings
    - Majority RAC Vote For A Public Hearing
THE RAC: TO BE OR NOT TO BE

- Reply from Dr. Jorgenson: 1-11-2016
  - NIH is streamlining the RAC process
  - NIH is currently analyzing Federal Register comments
  - NIH will publish final policy in the next several months
THE RAC: TO BE OR NOT TO BE

○ THE FATE OF THE VORINOSTAT + AGS-004 PROTOCOL:
  ○ MORE DATA REQUESTED AT 12-4-15 PUBLIC HEARING
  ○ SPONSOR FELT QUESTIONS POSED WERE ALREADY ANSWERED
  ○ FINAL 12-17-15 RAC LETTER MADE SEVERAL VERY SIMPLE RECOMMENDATIONS RE: QC OF TRANSFERRED RNA AND IC.
  ○ OK FROM DAIDS ON 2-8-16 TO ENROLL THE FIRST PATIENT
THE RAC: TO BE OR NOT TO BE

THANKS

- JEFF SHEEHY, MDC CARE CAB
- DAVE MARGOLIS AND CYNTHIA GAY, UNC
- HANS-PETER KIEM, FHCRC SEATTLE & RAC CHAIR