Slides for Break Out Session

NIST VCAT 8/14/2007

VCAT Subcommittee on Biosciences and Healthcare

- Review of recent NIST activities
  - FY 2008/2009 budget requests
  - NIST/UBMI Workshop
  - Physics Laboratory Biophysics initiative
  - ITL initiatives
- Discussion
- VCAT industry sector overview
  - Pharma/Drug Development
  - Diagnostics
- Discussion

Health Care, Biotechnology, Life Science NIST Strategic Planning: Straw man Process

- Outline industrial sectors
- Define critical measurements/technologies in sector
- Identify opportunities for advances in measurement science and development of critical standards
- Prepare summary
- Solicit input and comment from industry leaders
- Work with NIST staff to develop implementation plan

Example:
Health Care Industry sub-Sector

- Health Care
  - Drug Development
  - Diagnostics
  - Medical Devices
  - Services
- Biotechnology
  - Energy
  - Food products
  - Materials
- Life Science Research
  - Instrumentation, devices, and reagents for research
- Homeland Security
  - Forensics
  - Biometrics
  - Biohazard detection

Major Industry Sectors Based on Bio and Medical Sciences

- Health Care
  - Diagnostics
  - Drug Development
  - Medical Devices
  - Services
- Biotechnology
  - Energy
  - Food products
  - Materials
- Life Science Research
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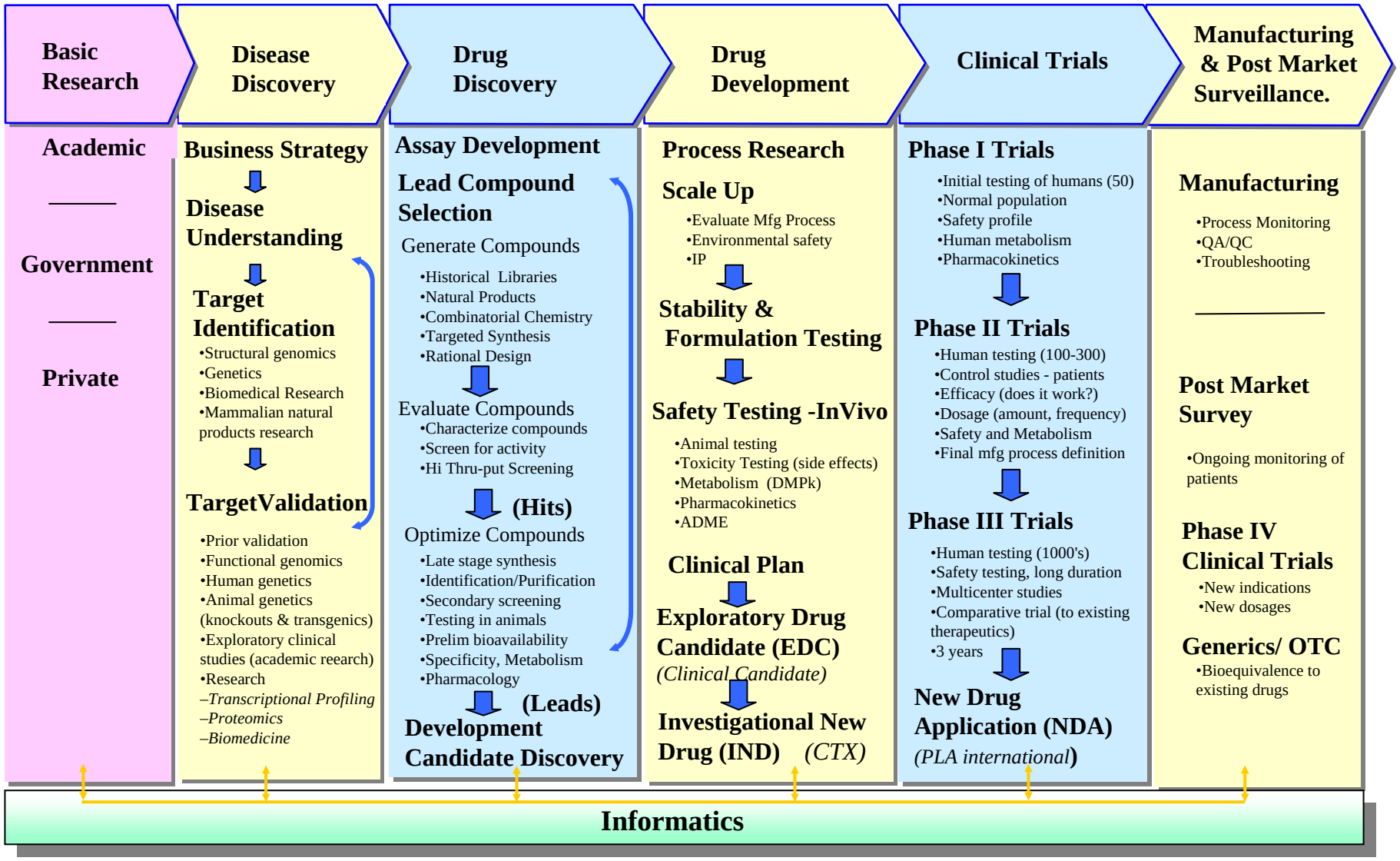
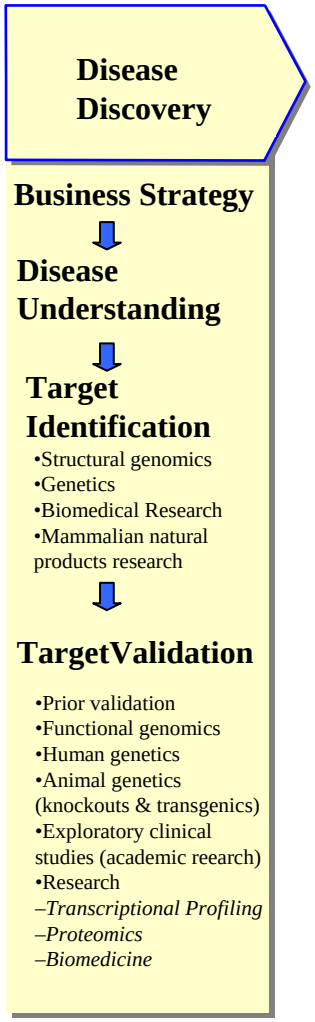
Pharmaceutical Value Chain



Pharmaceutical Discovery/Development

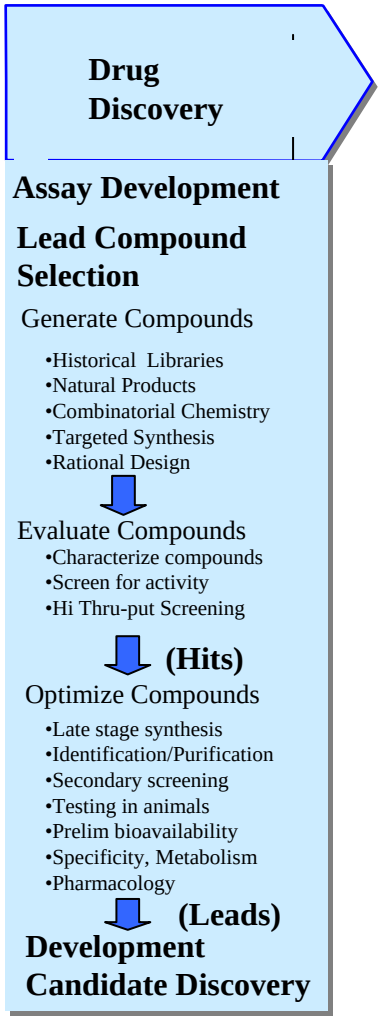
- It takes 13-15 years to bring a major drug to market
- It costs between $800M – $1 Billion dollars
- Only 1 in 10,000 compounds that are tested become a drug
- Failures caused by
  - Lack of sufficient efficacy
  - Toxicity
  - Metabolism

Key issues for Target ID/Validation



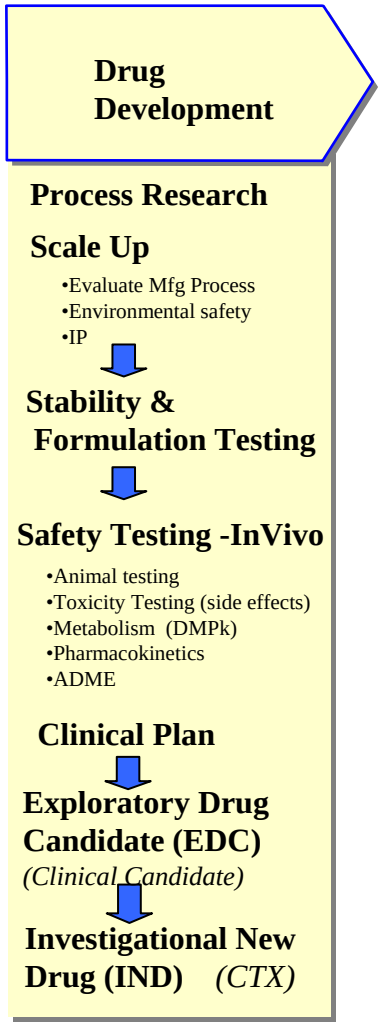
- Understanding of biological pathways of the disease (e.g. systems biology)
  - To identify an appropriate target(s) for intervention
- Critical measurements: Gene expression (DNA, RNA, Proteins, Metabolites)

Measurement Needs for Drug Discovery



- High throughput screening and other screening
  - To evaluate compounds for activity using protein and cellular based assays
- Determining ADME, Toxicity characteristics
- Critical measurements:
  - High sensitivity measurements
  - Protein binding
  - Cellular activity
  - Early stage toxicity

Measurement Needs for Drug Development



- In vivo testing in animals
  - Toxicity
  - ADME (Pharmacokinetics)
    - Absorption, Distribution, Metabolism, Excretion
- Critical measurement needs:
  - …..
  - …..

Measurement Needs for Clinical Trials

Clinical Trials

Phase I Trials

- Initial testing of humans (50)
- Normal population
- Safety profile
- Human metabolism
- Pharmacokinetics

Phase II Trials

- Human testing (100-300)
- Control studies - patients
- Efficacy (does it work?)
- Dosage (amount, frequency)
- Safety and Metabolism
- Final mfg process definition

Phase III Trials

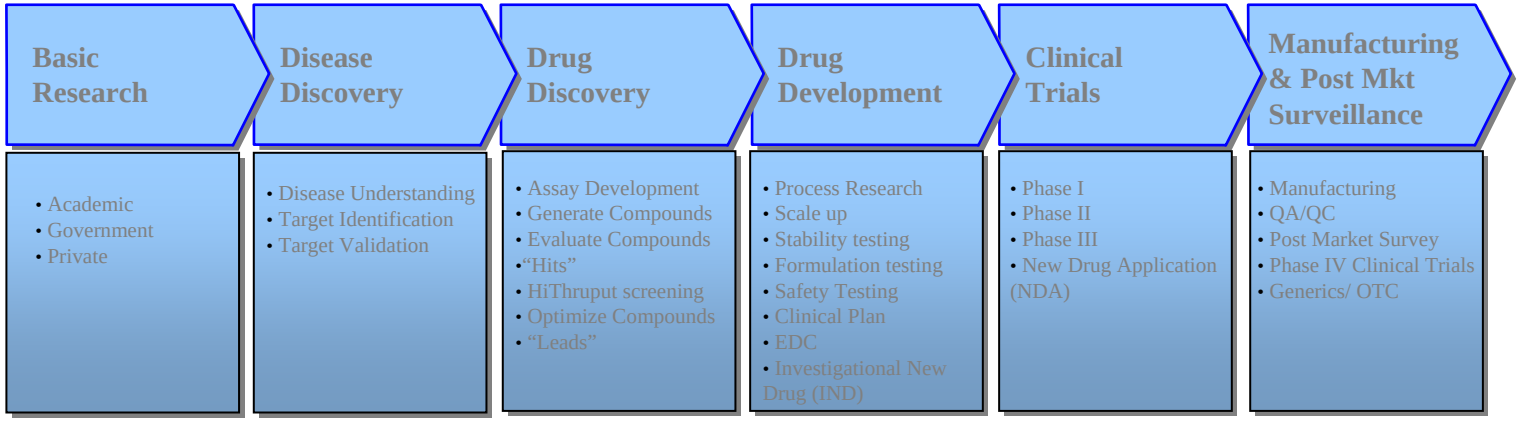
- Human testing (1000's)
- Safety testing, long duration
- Multicenter studies
- Comparative trial (to existing therapeutics)
- 3 years

New Drug Application (NDA)
(PLA international)

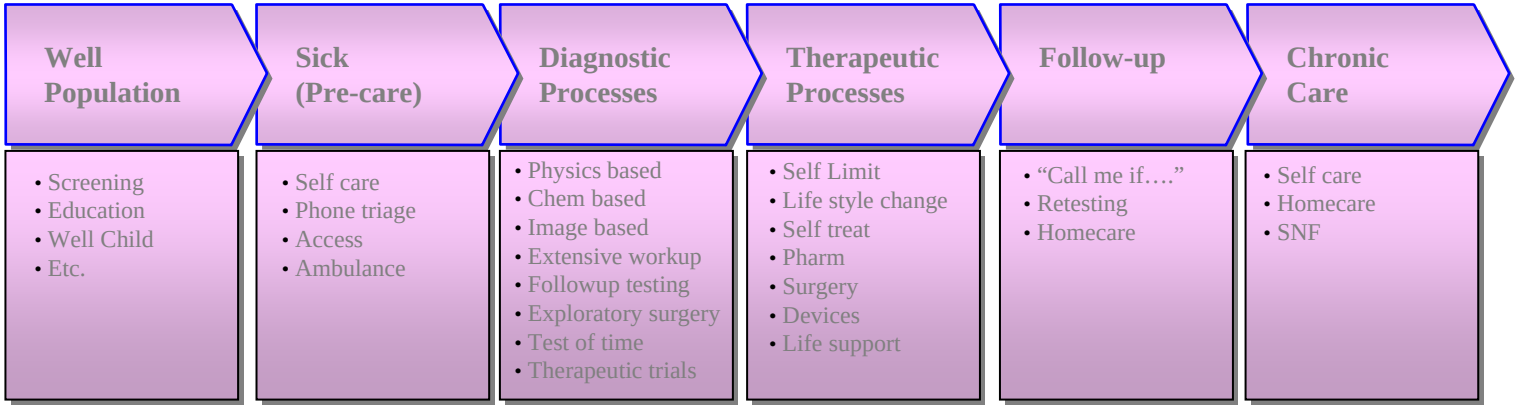
- Determine effect of drug candidate on humans
  - The effect on each human is different and determined by genetics
  - Patient stratification by genetic profile improves outcomes
- Critical measurements:
  - Rapid DNA testing for all persons in clinical trials

Integration of Measurements for Pharma and Diagnostics

Pharmaceutical



Diagnostic



Key Trends on the horizon for the Pharmaceutical Industry

- **Personalized Healthcare**
  - Getting the right medicine to the right patients at the right time
- **Continued Drive for Highly Innovative New Medicines**
  - Better understanding of disease pathways
- **Discovery and Enablement of the "Next big thing" in drug discovery**
  - Historical example : Monoclonal Antibodies
  - Future opportunity : Therapeutic RNAi?

Technology Platforms that could influence the Trends

- **Imaging**
  - Goal is to use technologies that are non-invasive to the patient
  - Biomarkers can provide the predictive information of disease and patient stratification
    - Currently use plasma samples, tumor biopsy and gene arrays with the exact method depending on the disease area

  Any increase in image resolution and quantitative measurement tools associated with imaging techniques may aid in improved disease diagnosis and treatment

- **Mass Spectrometry Technologies**
  - Analysis of proteins which is important for biomarkers and path ways for new medicine
  - We can analyze gene expression (RNA) with gene array chips, but no equivalently robust platform for proteomics
    - We cannot survey post translational modifications with adequate speed and sensitivity

  Need increased sensitivity and analyze multiple samples in parallel,
  Other technology platforms might also be applicable to proteomics

- **Delivery Technology for Oligonucleotides**
  - Examples of what is being looked at to do this are liposomes and nanoparticles

  All efforts to improve ability to deliver olignoculotides is key for new areas of disease management

Personalized Medicine

- The approach is to truly understand disease at the individual patient level

- Driving Forces
  - Improved efficacy to every patient and reduce side effects
  - Minimize or eliminate drugs going to patients where it will not help based on their individual biology
  - Cost of health care and insurance focus on not paying for care if efficacy can not be demonstrated

Innovative New Medicines

- Driving Force:
  - The biological pathways underlying several of the major diseases are still not understood
  - The sequencing of the human genome and the development of gene chips for analysis of messenger RNA has facilitated assessing the underlying biology, however, measurement of post translational protein modifications is still tedious

Opportunity for Mass Spectrometry, protein on chips, antibody arrays and other Proteomics Technologies

Diagnostic Industry Sectors

In Vitro Diagnostics

Discovery:
- Medical Schools, NIH
- Pharma R & D
- IVD R & D

Product Development:
- IVD Companies

Distribution Channels:
- Commercial Clinical Labs
- Hospital Clinical Labs
- Point of Care
  - Doctors office
  - Emergency room
  - Hospital bedside

Diagnostic Imaging

Discovery:
- Medical Schools, NIH
- Instrument manufacturers

Product Development:
- Instrument manufacturers

Distribution Channels:
- Imaging centers
- Radiology Departments
- Doctor's offices

Vital Signs Monitoring

Discovery:
- Medical Schools, NIH
- Instrument manufacturers

Product Development:
- Instrument manufacturers

Distribution Channels:
- Point of Care
  - Patient bedside
  - Surgical suites
  - Doctor's offices
  - ER
  - EMT

21st Century Diagnostic Medicine

- **Predict:** Determine disease proclivity
  - DNA SNP pattern
  - Family history
- **Screen:** Detect early for effective intervention
  - Imaging
  - Body fluid trace analysis
- **Diagnose:** Precisely specify disease phenotype to choose optimal therapy
  - Molecular analysis
  - Imaging
- **Monitor:** Measure response to therapy and provide early detection of recurrence
  - Imaging
  - Body fluid trace analysis

Predict Disease Proclivity

- DNA SNP and mutation analysis
  - Nucleic acid sequencing
- Protein biomarkers in blood
  - Protein mass spec and correlations
- Metabolites in blood, urine, and tissue
  - Trace element analysis

Screen

- Imaging
  - Cancer early detection
    - CT, MRI, US, OCT quantitative imaging
  - Coronary artery disease
  - Embolisms
- Blood testing
  - Hematology
    - Immune system
      - Flow cytometry
  - Blood chemistry
    - Protein biomarkers of disease
      - Protein Mass Spec
  - Metabolics
    - Diabetes
      - ELIZA, blood chemistry analysis

Diagnose

- Tumor molecular phenotype analysis
  - Microgenomics
    - DNA microarrays, Q-PCR, NA amplification
  - Micro-proteomics
    - Protein mass spec, protein arrays, ELIZA
- Imaging
  - Tumor size and shape
    - Feature extraction and quantitation
    - Functional characteristics
      - Functional biomarkers for MRI and CT
- DNA mutation analysis
    - SNP arrays, high throughput sequencing, amplification
- Blood testing
  - Trace chemical analysis
    - Mass Spec

Monitor Treatment response

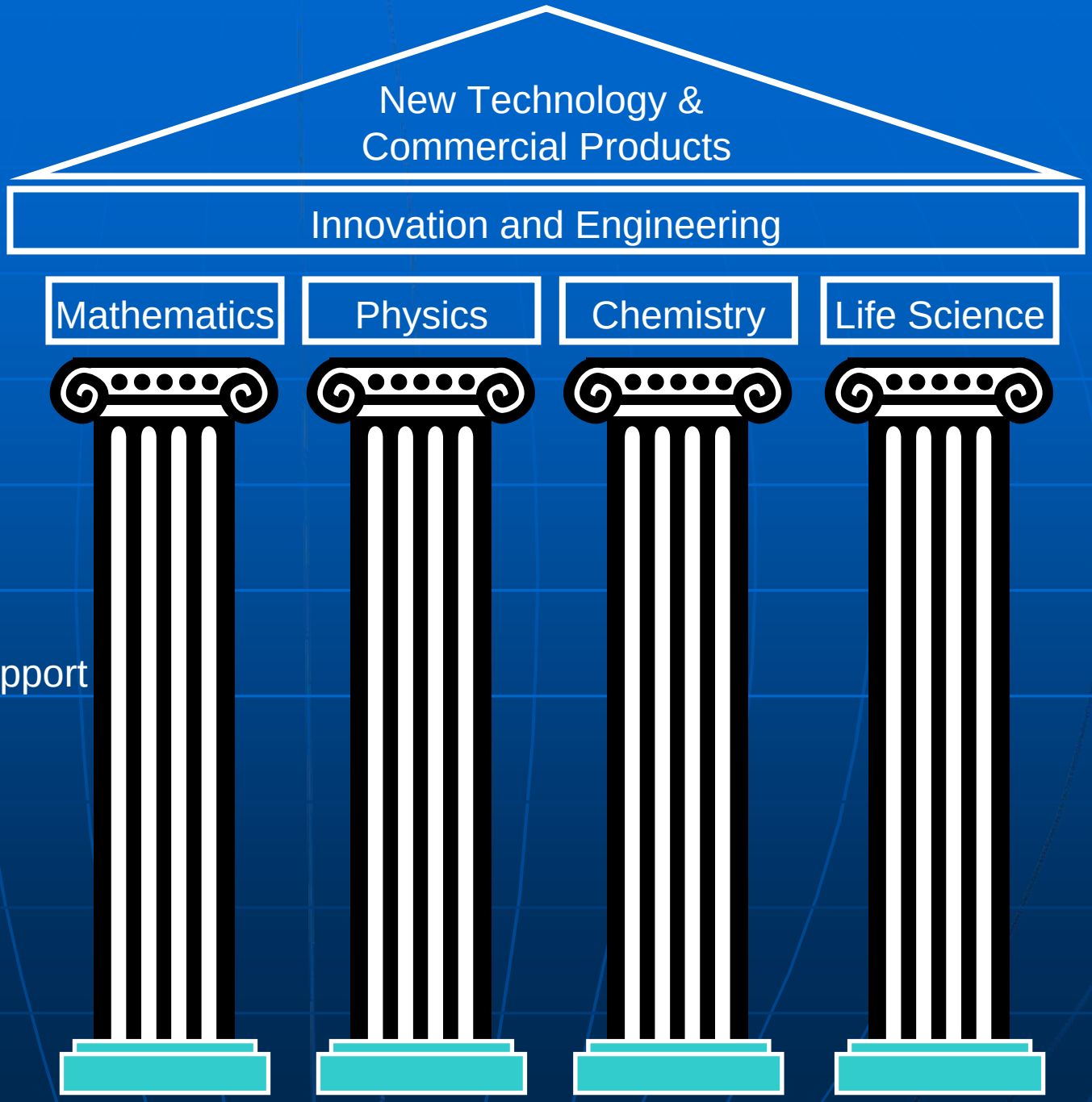
- Imaging
  - Tumor size/morphology changes for drug response
    - Quantitative imaging
- Blood tests
  - Chronic disease management
    - Aids: Flow cytometry, viral load
    - Diabetes: Glucose levels
    - Stroke: Blood clotting levels
    - Cancer: Rare cell detection, proteomics (?),

The NIST Approach?

- Identify under served areas of US industry
- Identify available NIST resources
- Evaluate core competences
- Determine industry sectors where these individuals can make a significant contribution
- Formulate a NIST research program

The VCAT Approach?

- Identify under served areas of US industry
- Determine and prioritize critical measurement needs
- Define skills that best address these measurement needs
- Find suitable staff at NIST, partner with other groups, hire in skills
- Formulate strategic plan



Can NIST, as currently structured, Adequately support US Biotechnology And Healthcare Industries?

Strategic Planning Process

- Develop program portfolio
  - Near-term, 25% resources
  - Mid-term 50% resources
  - Long-term 25% resources