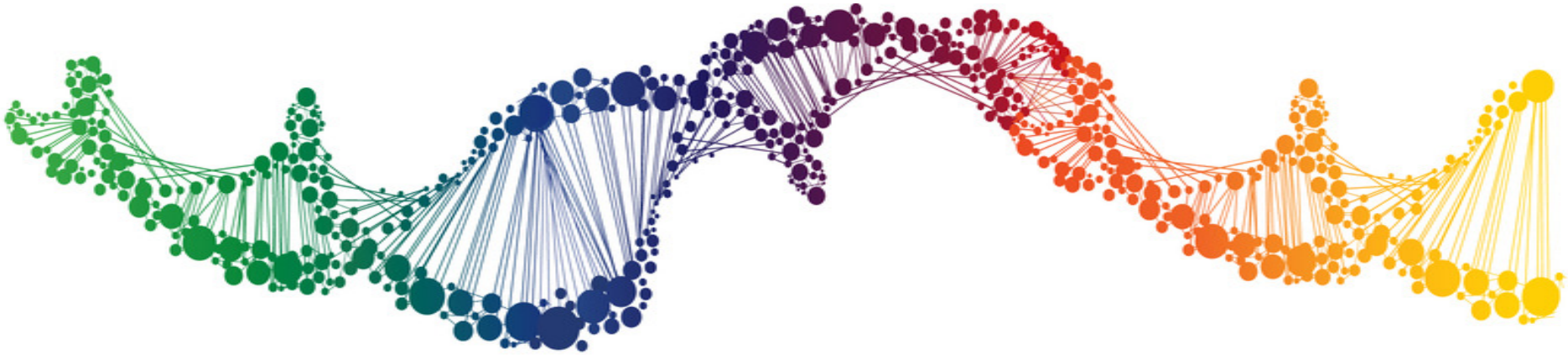
BCA Blood Centers OF AMERICA

2018 BCA IRL Networking Conference

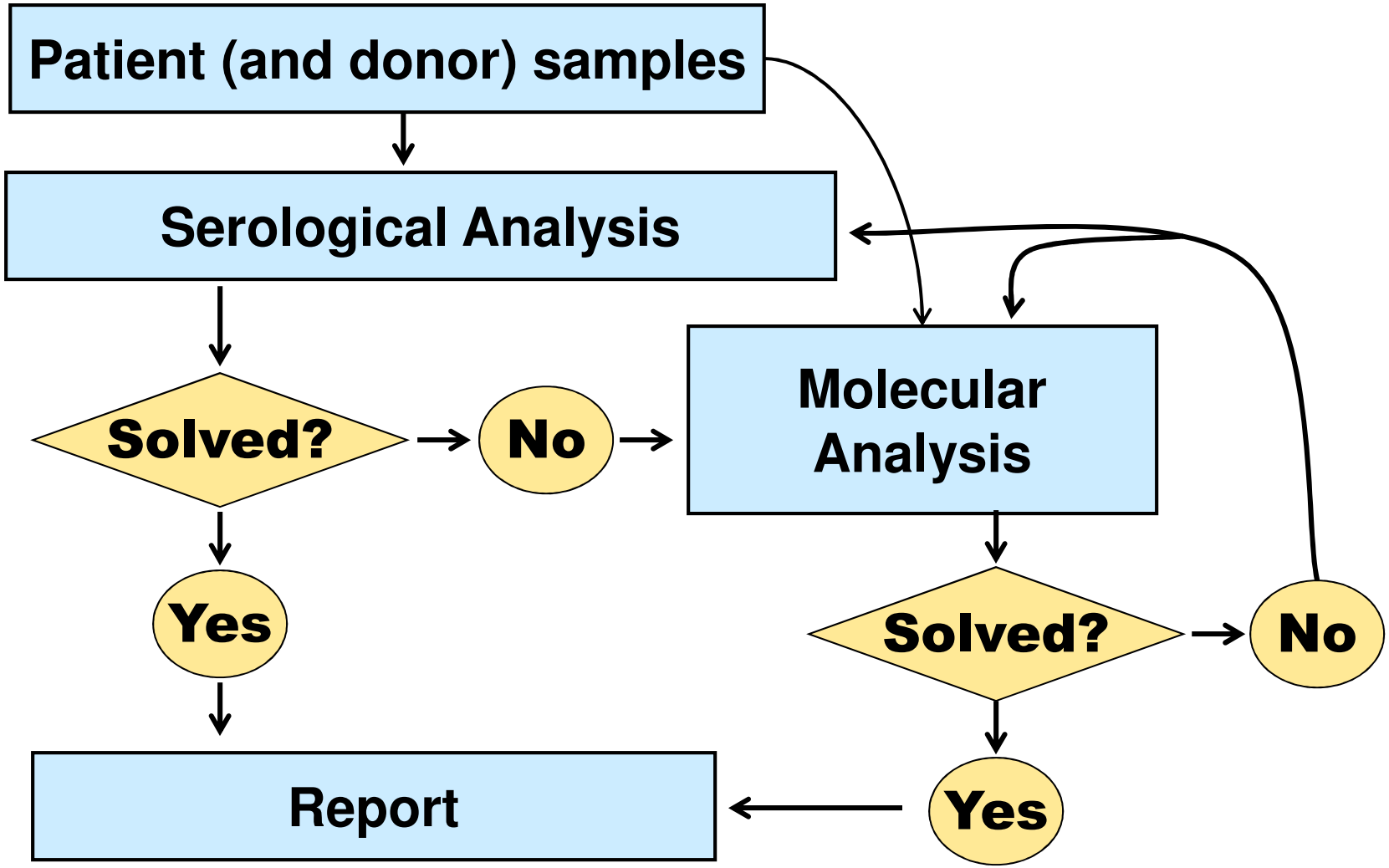
DNA testing of patients and donors

Sunitha Vege
Genomics Laboratory
New York Blood Center

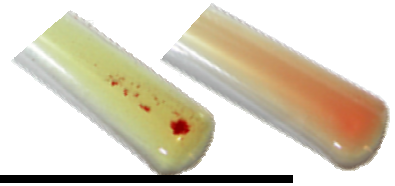


New York Blood Center | Community Blood Center | INNOVATIVE BLOOD RESOURCES | Rhode Island Blood Center | Blood Bank of Delmarva

DNA ANALYSIS AND HEMAGGLUTINATION: A POWERFUL PARTNERSHIP



TRADITIONAL SEROLOGICAL TOOLS



- Hemagglutination to test serum and RBCs
  - Simple, inexpensive, and when done correctly, has a specificity and sensitivity that is appropriate for most testing
  - Potentiators: e.g. albumin, LISS, and PEG, to enhance weakly reactive antibodies
  - Phases of reactivity (e.g., 4C, RT, 37C, IS, IAT, DAT)
  - Enzymes and chemicals: papain, ficin, α-chymotrypsin, trypsin and DTT to provide information about the antigen
  - Extensively typed RBCs for routine and selected panel(s)
  - RBCs with null phenotypes to test with patient's serum/plasma
  - Typing of patient's RBCs for common and high/low prevalence antigens
  - Absorption and elution

➢ But these "traditional" tools are subjective, labor intensive, and an "art "

New York Blood Center | Community Blood Center | INNOVATIVE BLOOD RESOURCES | Rhode Island Blood Center | Blood Bank of Delmarva

ADVANTAGES OF DNA TESTING

- Type multiply transfused patients
  - DNA isolated from white cells
  - no interference from transfused cells
- Type RBCs coated with immunoglobulin (+DAT)
  - Alternative – chemical treatment
  - Labor intensive
- Type when no commercial reagents
  - Dombrock $Do^{a/b}$, Hy, Jo^{a}, Kell system $Js^{a/b}$, V/VS, U, hr^{S}/hr^{B}, etc.
- Determine RHD zygosity (one copy or two copies of D)
  - Test paternal sample when OB patient has anti-D to predict fetal risk for HDN
  - Typing fetus (amniocytes)

CAN DO SOME THINGS SEROLOGY CANNOT

- Distinguish weak D from partial D antigen
  - OB patients to determine if candidate for Rh immune globulin
  - Conserve D– blood supply
- Determine RH genotype, especially for patients with SCD
  - Determine which patients have partial D, partial C, or partial e
    - partial C: switch SCD patients to C negative transfusion protocol
  - Key for antibody identification and selection of donor units as these patients can have complex Rh antibodies
- Determine allo or auto antibody
  - Patient RBCs type positive for the antigen but has the corresponding antibody in the plasma
  - Example: Jk(a+) with anti-Jka
- Resolve ABO discrepancies and determine A2 subtype
  - A_2 subtype for kidney and organ transplants
  - Discrepancy between forward and reverse type, between current and historic ABO, or weak typing

cmw3

NYBC PATIENT TESTING

- Every sample submitted for antibody work-up to the NYBC Immunohematoloy laboratory is reflexed to HEA BeadChip assay
  - Policy implemented in 2011 with HEA performed at reflex charge to customers
  - Hospitals were communicated months prior policy was implemented, during which the HEA was performed at no cost.
- If no indication of BMT or stem cell transplant, HEA assay is not repeated on a patient sample.
- Offer “DARA” workup for patients on monoclonal antibody therapies (commonly, anti-CD38):
  - Serology and HEA testing
  - Antigen matched unit also part of "package".
    - Some customers give antigen matched (Rh, K, Fy, Jk, S) and then don't repeat antibody workup during that hospital stay (medical decision).

New York Blood Center · Community Blood Center · IBR Innovative Blood Resources · Rhode Island Blood Center · Blood Bank of Delmarva

Slide 6

cmw3 again, avoid "reduced rate" comment....just call it part of DARA workup package or some such.

Antigen matched unit also part of "package". some of our customers give antigen matched (Rh, K, Fy, Jk, S) and then don't repeat antibody workup during that hospital stay (is medical decision).

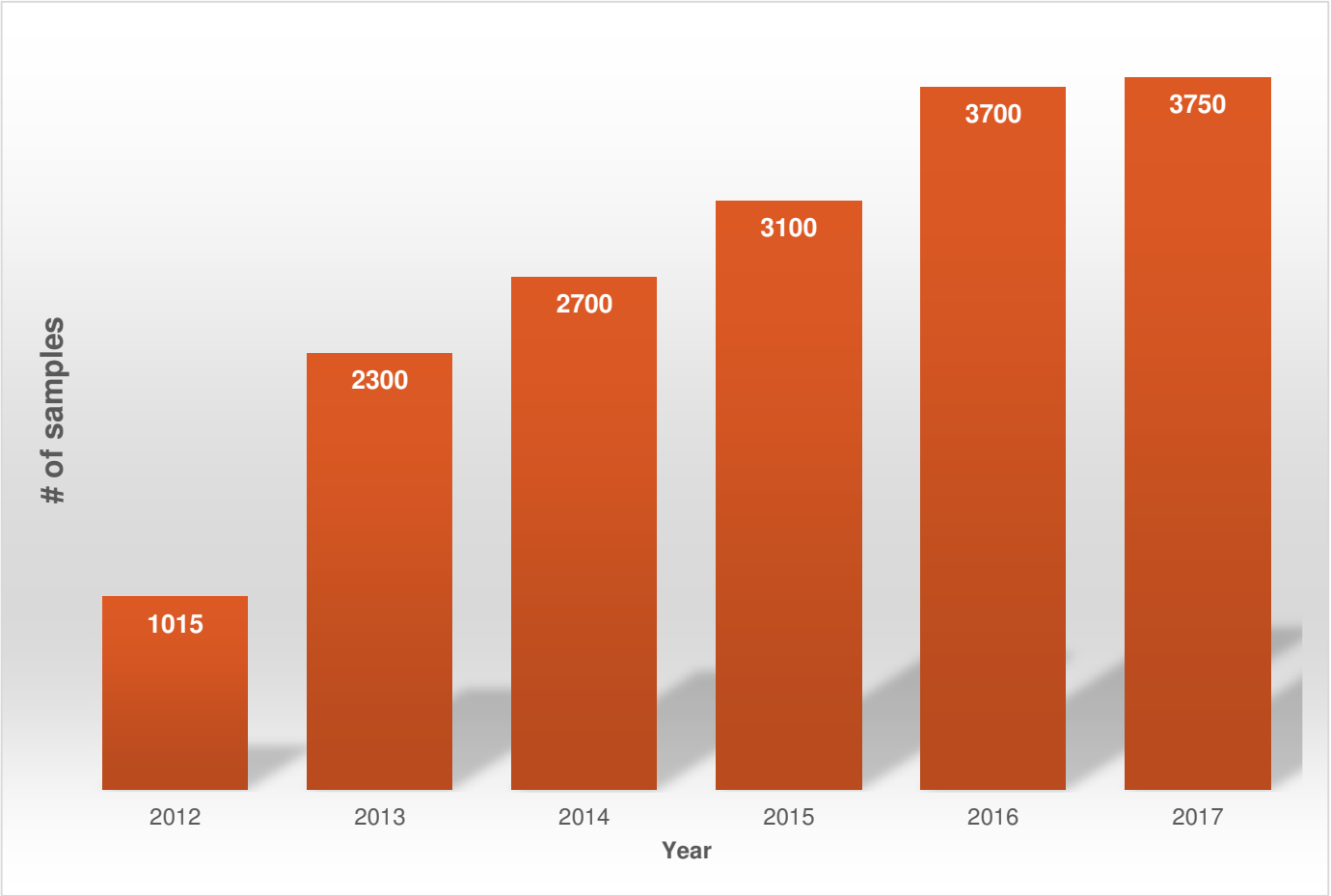
Connie Westhoff, 6/19/2018

NYBC PATIENT REFERRALS

- Majority of the requests:
  - Common red cell profile - HEA PreciseType panel
  - Weak vs partial D
  - Unexpected Rh antibodies
  - Full RH genotype; commonly sickle cell patients
  - ABO genotype; for A2 and discrepancy resolution
  - RHD zygosity for prediction of risk of HDFN
- Less common:
  - Unexpected antibodies or weak antigen expression in other blood groups
    - JK, KEL, DO, FY, LU, etc
  - Testing of amniocytes
  - McLeod testing
  - NAIT cases - HPA testing

New York Blood Center | Community Blood Center | IBR Innovative Blood Resources | Rhode Island Blood Center | Blood Bank of Delmarva

SAMPLE NUMBERS FOR DNA TESTING



New York Blood Center

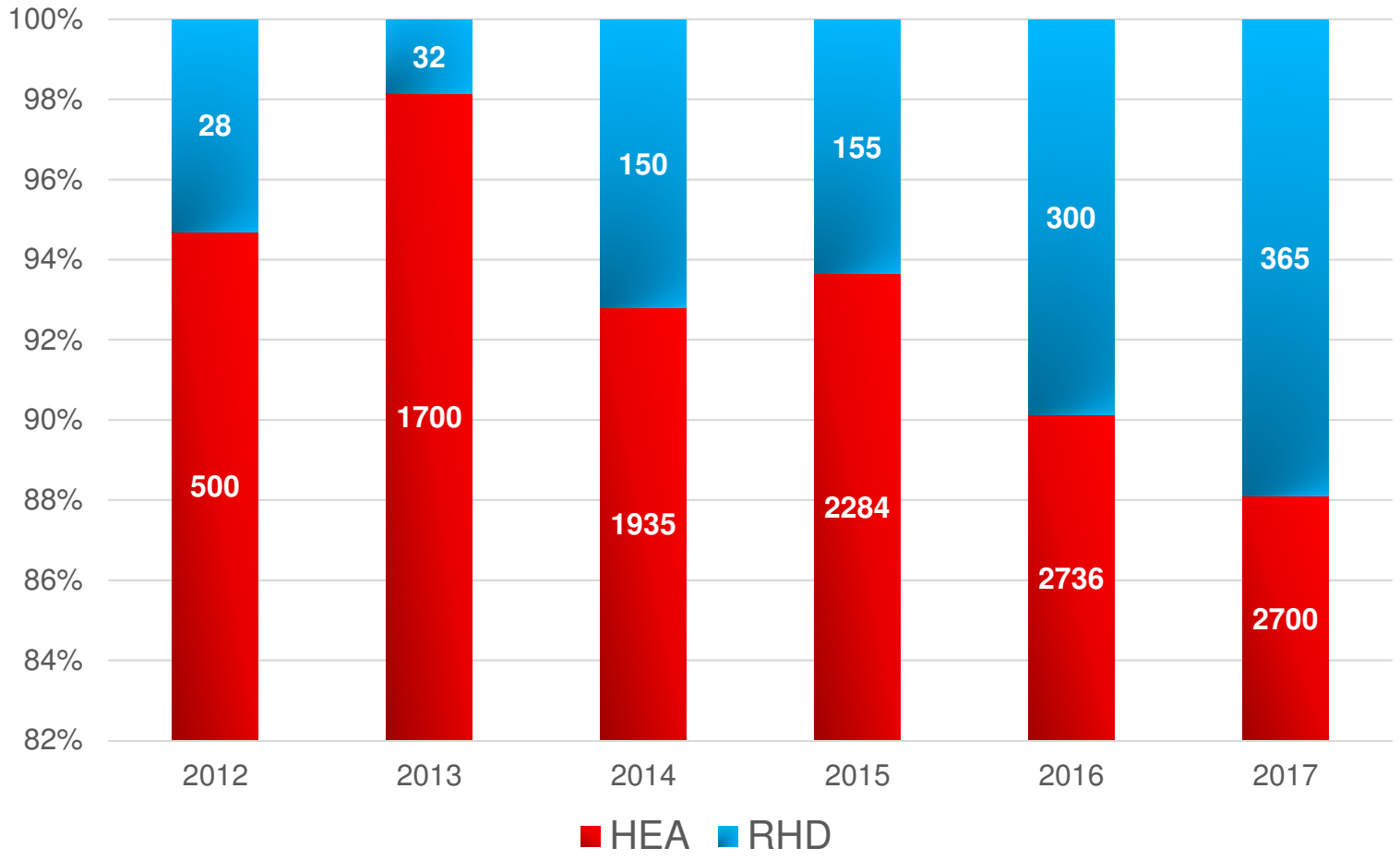
Community Blood Center

INNOVATIVE BLOOD RESOURCES

Rhode Island Blood Center

Blood Bank of Delmarva

HEA AND RHD REQUESTS



New York Blood Center

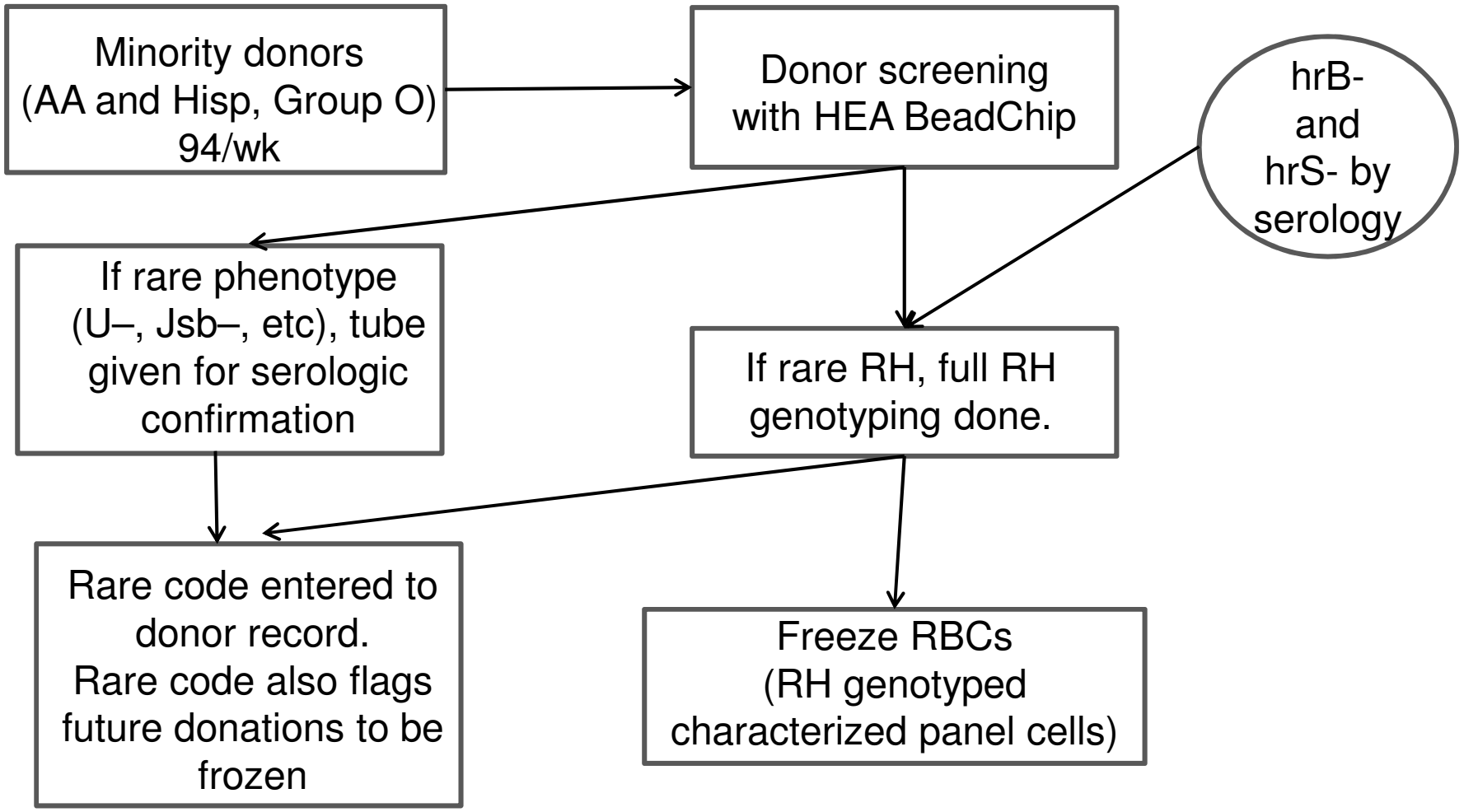
Community Blood Center

IBR INNOVATIVE BLOOD RESOURCES

Rhode Island Blood Center

Blood Bank of Delmarva

NYBC PREVIOUS DONOR TESTING STRATEGY



New York Blood Center · Community Blood Center · INNOVATIVE BLOOD RESOURCES · Rhode Island Blood Center · Blood Bank of Delmarva

RARE PHENOTYPES

- From screening ~10,000 donors from 2011

Phenotype	#
hr^B–	400
U–	25
U+var	19
Jo(a–)	44
Hy–	12
Js(b–)	36
k–	2
Lu(b–)	7
Di(b–)	3
Co(a–)	1

→ ~50 addl known hr^B- by serology

New York Blood Center · Community Blood Center · INNOVATIVE BLOOD RESOURCES · Rhode Island Blood Center · Blood Bank of Delmarva

CURRENT RH TESTING

- RH genotyping performed:
  - Immucor
    - RHD BeadChip
    - RHCE BeadChip
  - Lab developed tests:
    - [illegible] covered by BeadChip
      - ➢Labor and time intensive!
      - [illegible] alleles: PCR-RFLP for 1136C>T
    - RHCE*ceAG allele: PCR-RFLP for 254C>G
    - AS-PCR for hybrid *RHD*DIIIa-CE(4-7)-D* (r'S)
    - DNA sequencing if needed

New York Blood Center · Community Blood Center · INNOVATIVE BLOOD RESOURCES · Rhode Island Blood Center · Blood Bank of Delmarva

INDUSTRY OVERVIEW

Decline in blood usage has precipitated

- Competitive pressures in the industry
- Decrease cost recovery for core blood products

OPPORTUNITY – extended antigen typed units

- Potential area of growth & revenue generation for blood centers
  AND
- Improve patient care

CHALLENGE - providing extended antigen typed

- Currently: Labor intensive
  Primarily manual methods
  Activity falls to IRL

New York Blood Center · Community Blood Center · IBR Innovative Blood Resources · Rhode Island Blood Center · Blood Bank of Delmarva

CENTRALIZED TESTING MODEL

Genomics approach offers lower cost

- labor, reagents, and higher throughput

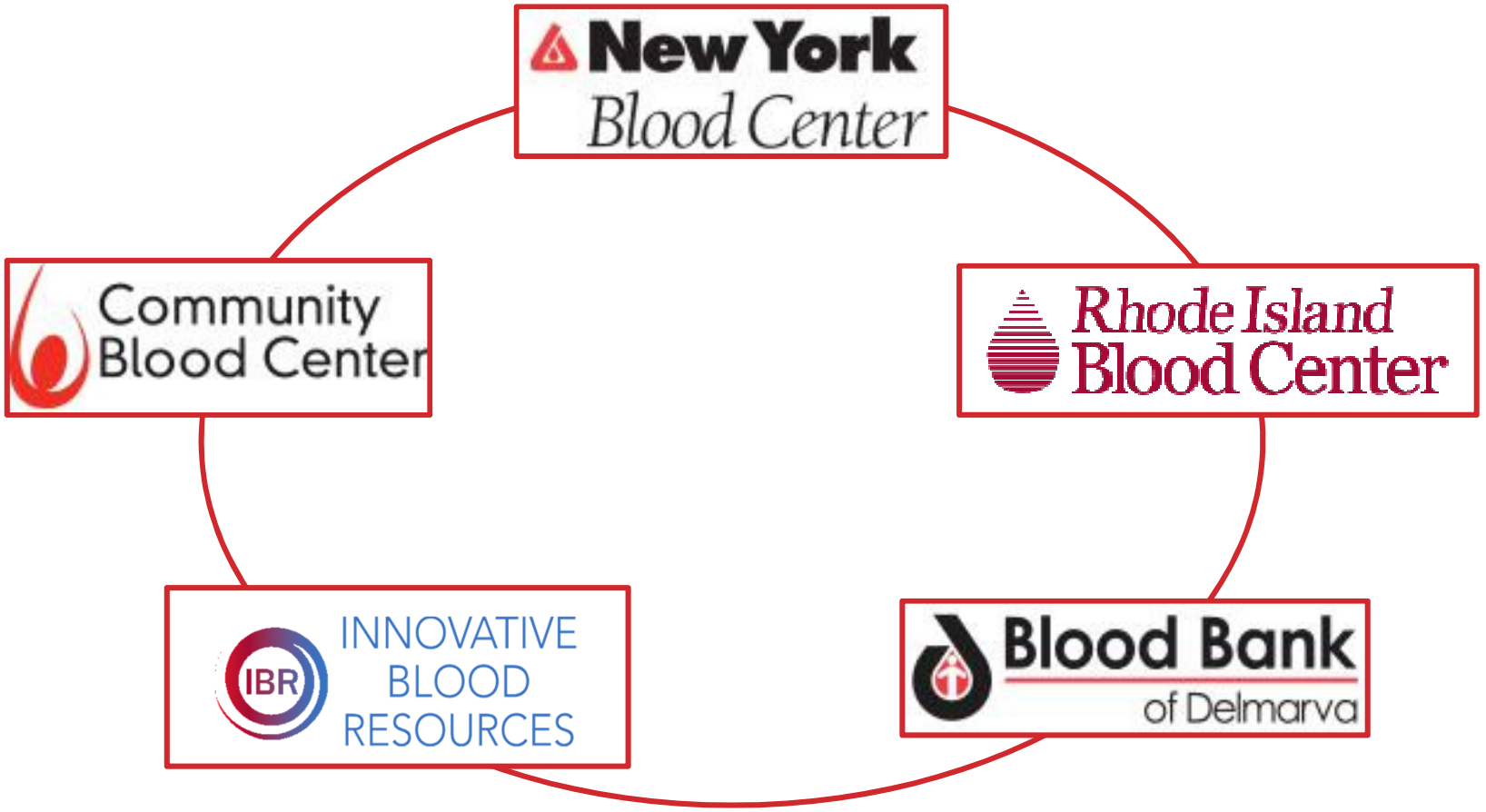
Improved accuracy

- all antigens of interest can be tested in a single assay
- electronic transfer to donor record
- electronic labeling

Keep highly trained IRL staff for complex testing

New York Blood Center | Community Blood Center | IBR Innovative Blood Resources | Rhode Island Blood Center | Blood Bank of Delmarva

NYBC ENTERPRISE



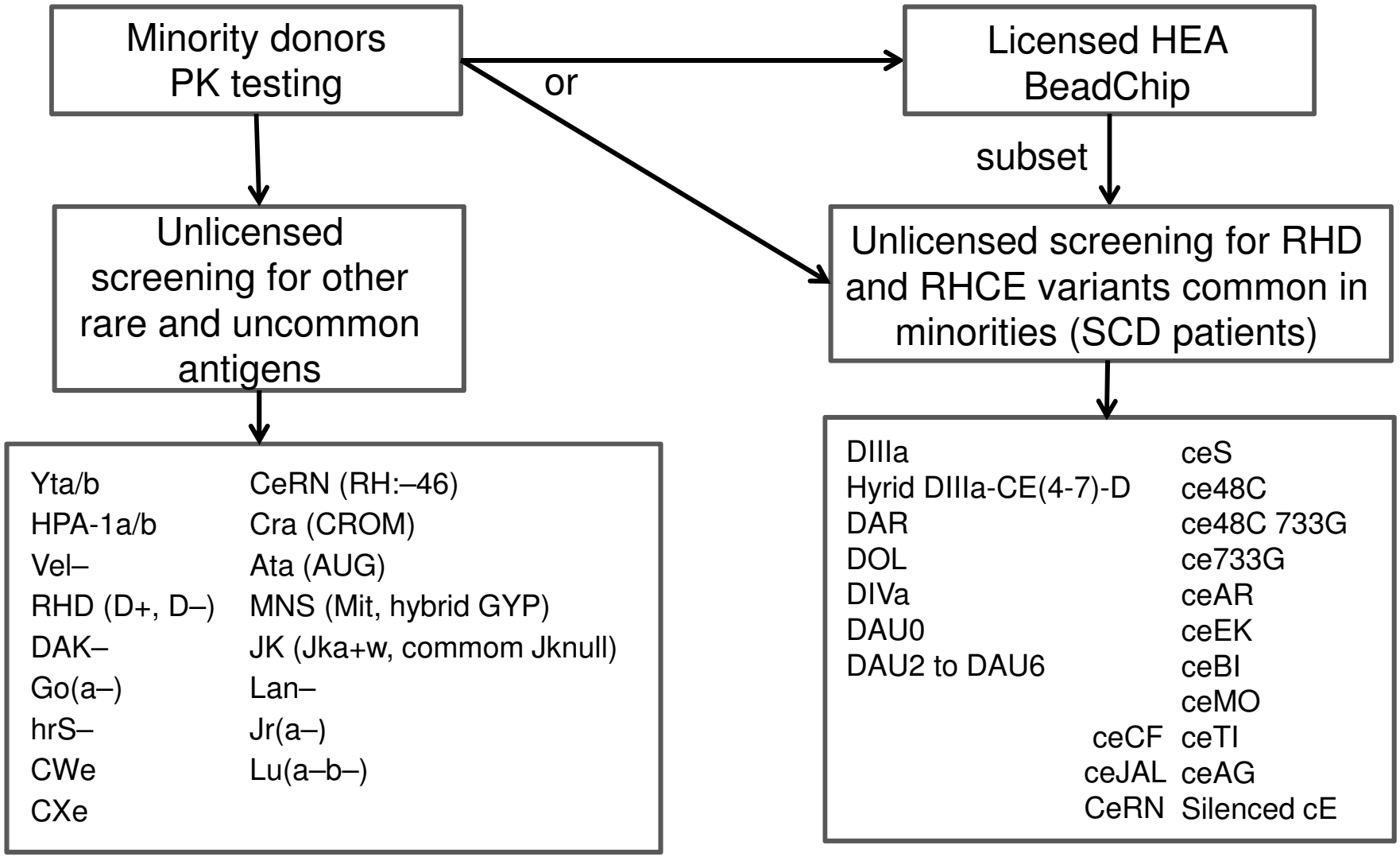
New York Blood Center
Community Blood Center
INNOVATIVE BLOOD RESOURCES
Rhode Island Blood Center
Blood Bank of Delmarva

NATIONAL CENTER FOR BLOOD GROUP GENOMICS

Donor testing for NYBC partner laboratories and other blood centers nationwide

- Test donor samples on PK7300 for low cost for Rh and K
- Reflex donors to HEA testing – Group A and O
  - R1 (non-caucasian)
  - O negative; rr (non-caucasian)
  - All R2 and R0, then R1
- HEA test results are interfaced with blood center donor LIS system; no manual entries
- Greatly increase the supply of antigen negative donor units available for patient need
  - Goal to screen 500 donors per week by HEA assay

NEW STRATEGIES FOR DONOR TESTING



New York Blood Center · Community Blood Center · INNOVATIVE BLOOD RESOURCES · Rhode Island Blood Center · Blood Bank of Delmarva

RH DONOR SCREENING

- Unlicensed high-throughput assay for RH molecular characterization of donors
  - Reduce cost to genotype by reducing labor and time
- More streamlined process of donor testing
- RH genotyped donors in inventory as liquid units
  - Freeze RBCs from retention tubes for panel cells
    - RH genotypes of varying antigen profiles
- Integrate RH genotypes into donor records

New York Blood Center | Community Blood Center | IBR INNOVATIVE BLOOD RESOURCES | Rhode Island Blood Center | Blood Bank of Delmarva

GOAL: "OPERATIONALIZE" PRECISE MATCHING

Bring Genomics to Transfusion with "economy of scale"

Testing patients

- improve patient care
- one time testing
- part of medical record

Testing Donors

- linked to donor record

= ++Price Point

New York Blood Center · Community Blood Center · INNOVATIVE BLOOD RESOURCES · Rhode Island Blood Center · Blood Bank of Delmarva

QUESTIONS?