

# The CRMGEN Project

## Certified Reference Materials for Molecular Genetic Testing

David Barton

National Centre for Medical Genetics

Dublin, Ireland

# Prioritization

- In principle, RMs are required for every mutation in every gene
- This is not realistic at present, so we must decide which RMs to produce first.
- We are looking for **MAXIMUM IMPACT** for the limited resources available for RM production

# Prioritization of RM Development 1

- The number of potential users of the RM
  - User surveys: Labs, developers, regulators
  - Current usage patterns
  - Predicting the future – expert input
- The geographical distribution of potential users of the RM
  - Ethnic panels
  - Local issues
- The availability or non-availability of RMs for the target at present
  - Expert knowledge
  - Regular contacts between experts
  - Catalogues
  - Web portals

# Prioritization of RM Development 2

- The existence of national or international guidelines on screening/testing for the target mutation(s)
  - Guidelines drive panel composition
  - Differences between guidelines
- The nature of the target mutation(s)
  - Affects format, cost
- The range of assays used to detect the target
  - Affects format, cost: commutability

# Prioritization of RM Development 3

- Problems identified in EQA for the target which could be solved by RMs
  - Immediate danger to patients
  - Links to EQA providers
- The availability of source materials for RM development
  - Existing materials (consent?)
  - Links to labs, clinics, patient organisations
- IPR issues; the existence of a patent on the target sequence
  - Potential to block RM production – real risk?
  - Cost of licensing
  - High cost of legal assessment

# The CRMGEN project - RMs

<b>Disorder</b>	<b>RMs to be developed</b>	<b>RM Type*</b>
Cystic Fibrosis	$\Delta$ F508, G542X, G551D, N1303K	CL
Haemochromatosis	C282Y, H63D, <u>S65C</u>	PCR
Fragile X syndrome	Normal, premutation, expansion	CL, gDNA
Sickle cell anaemia	HbS	PCR
Beta thalassaemia	Codon 39 (C->T), IVSI- 110 (G->A)	PCR
Factor V Defect	R506Q, Factor V "Leiden"	rDNA
HNPCC	Representative nonsense mutations	gDNA
DMD	Deletions, duplications	rDNA

\*KEY: CL, cell line; PCR, polymerase chain reaction product; gDNA, genomic DNA; rDNA, recombinant DNA