TIMETABLE

- REGISTRATION - COFFEE
- (9am) WELCOME AND HOUSEKEEPING
- INTRODUCTION and PORTFOLIO OVERVIEW
- (950am) BREAK
- PLASMA R&D
- rHDL
- (1150am) WRAP UP

CSL Limited R&D BRIEFING

DECEMBER 16, 2004

Dr. Andrew Cuthbertson

Dr. Jeff Davies

Dr. Russell Basser

R&D - Investment Objectives

1. Sustain a highly profitable plasma business.

2. Identify and develop novel products where we have Intellectual Property and insight.

3. Leverage our investment through partnering.

4. Contribute as part of a fully integrated, specialist biopharmaceutical company.

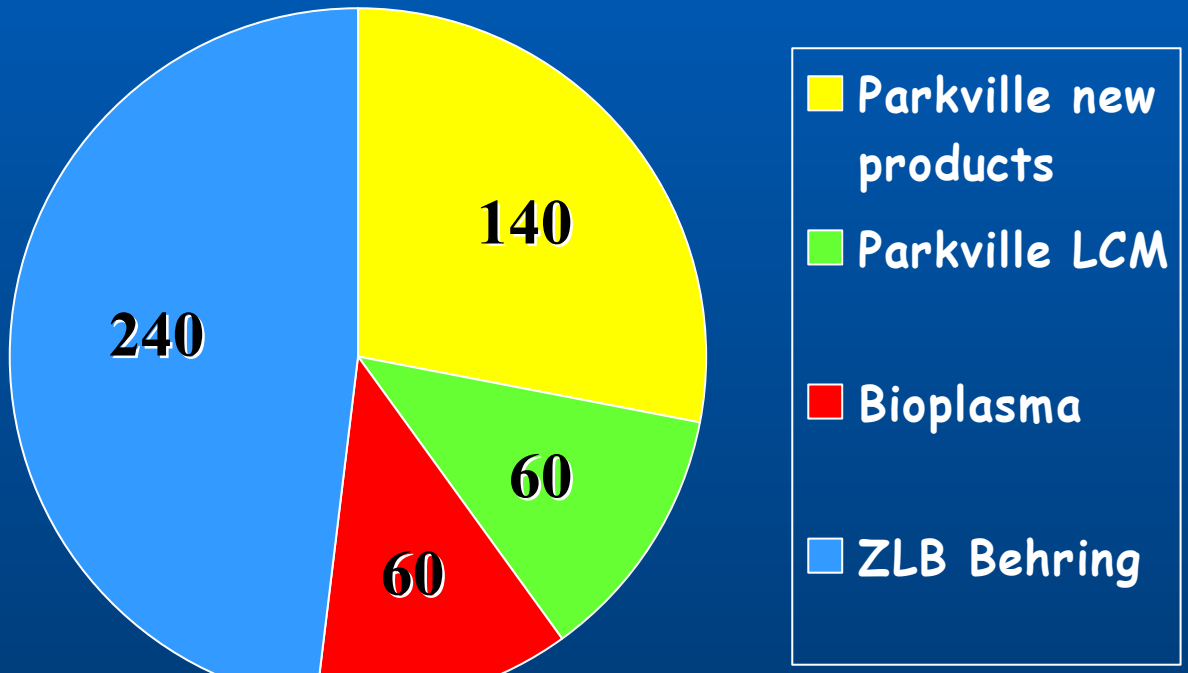
R&D Competitive Advantages

- Key competitive advantages
  - specialist focus
  - effective scale
  - attractive academic partner
  - CSL recruits high calibre scientists
- Impact of ZLB-Behring
  - global capability
  - centres of excellence aligned with manufacturing
  - synergies achieved

Commercially Driven, Integrated R&D

	CSL Group	ZLB Behring	CSL Bioplasma
• **Focus**	• **Novel protein product development** • Operations Support	• **Life cycle management plasma products** • Operations Support	• **Life cycle management plasma products** • Operations Support
• **Key Areas**	• Biotechnology • Recombinant proteins • Monoclonal antibodies • Vaccinology	• Immunology • Hemophilia • Wound Healing • Specialty products • A1PI	• New purification technologies
• **Laboratories**	• Parkville, Australia • Marburg, Germany • Bern, Switzerland	• Marburg, Germany • Bern, Switzerland	• Broadmeadows, Australia

R&D Staff and Budget



~500 staff
~A$140M

Integrated R&D Portfolio Management

R&D PORTFOLIO December 2004: Novel Protein Product Development

HPV Prophylaxis

- ISCOMATRIX
  - HCV
  - ESO-1
  - Dengue
  - Chlamydia

Clinical Trials

- rHDL
  - Stroke
  - ACS
- HPV Therapy

Preclinical Evaluation

- Topical Eye Delivery
- CRCs
- rMAbs

R&D PORTFOLIO December 2004: Plasma Products

Immunoglobulins

Coagulation factors

Specialty Products

HPV Vaccine Update

- Merck webcast Dec 14, 2004

http://www.merck.com/newsroom/webcast/

ISCOMATRIX® Adjuvant Technology New Milestones

- HCV: started safety study in chronically infected patients (Chiron)
- ESO1: publication of clinical immunogenicity data*. Started advanced disease study. Commitment to start definitive MRD study in 2005 (LICR)
- Chlamydia: new collaboration (Aventis Pasteur)
- Dengue: NIH preclinical/clinical grants (Hawaii Biotech)

* *Proceedings of the National Academy of Science (USA) 101:10697, 2004.*

ZLB Behring
Plasma Product R&D

Jeff Davies

Head of R&D Integration

Global Director of Plasma Product R&D,
ZLB Behring

ZLB Behring R&D has a key role in delivering on:

- a broad product portfolio with continuing innovation.
- development of high quality, high yielding efficient manufacturing processes.
- registrations to expand marketing reach.

Key Value Drivers for R&D Integration

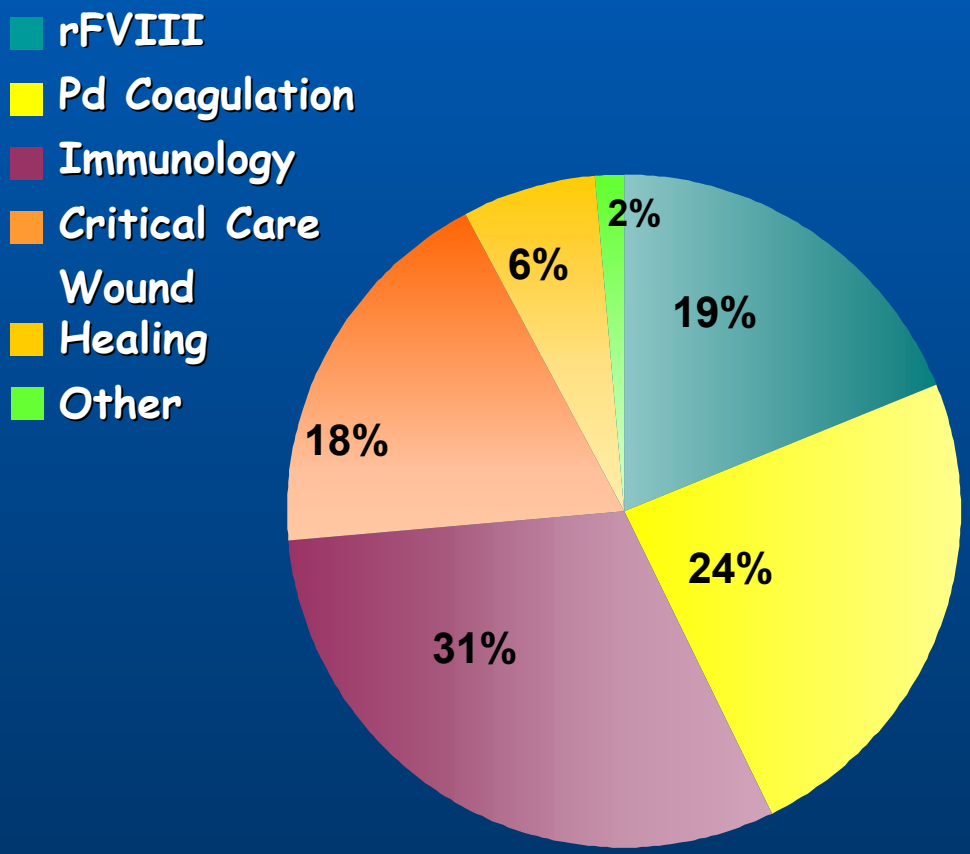
- R&D alignment with optimised manufacturing network:
  - Immunology (Bern)
  - Haemophilia, Specialty products (Marburg)
  - Alpha-1-Proteinase inhibitor (Kankakee)
- R&D alignment with Commercial Operations

R&D Integration is Well Advanced

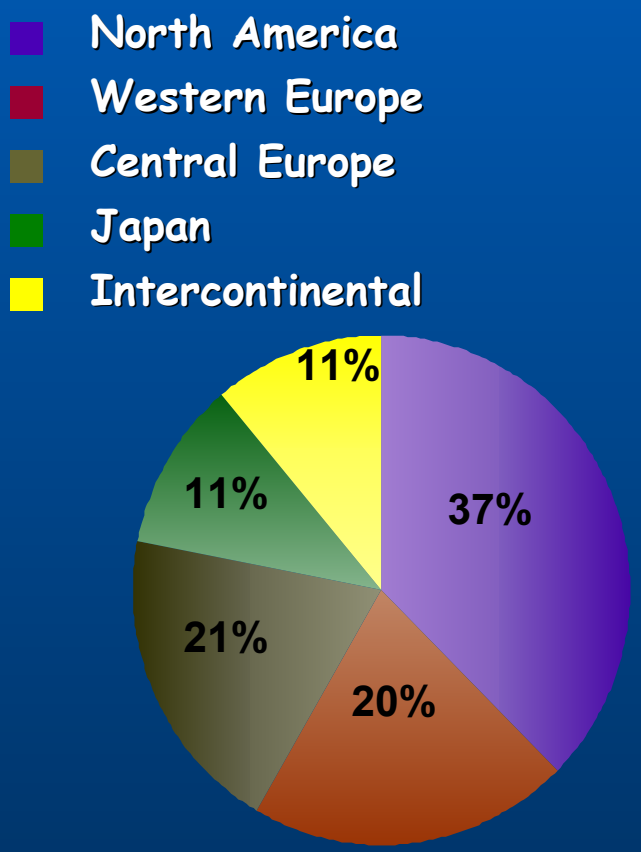
- R&D restructure completed
- Key project decisions made
- Financial targets on track
- Global management systems established

R&D Supports a Major Global Product Portfolio

Per Therapeutic Category % Total Sales



Per Region % Total Sales

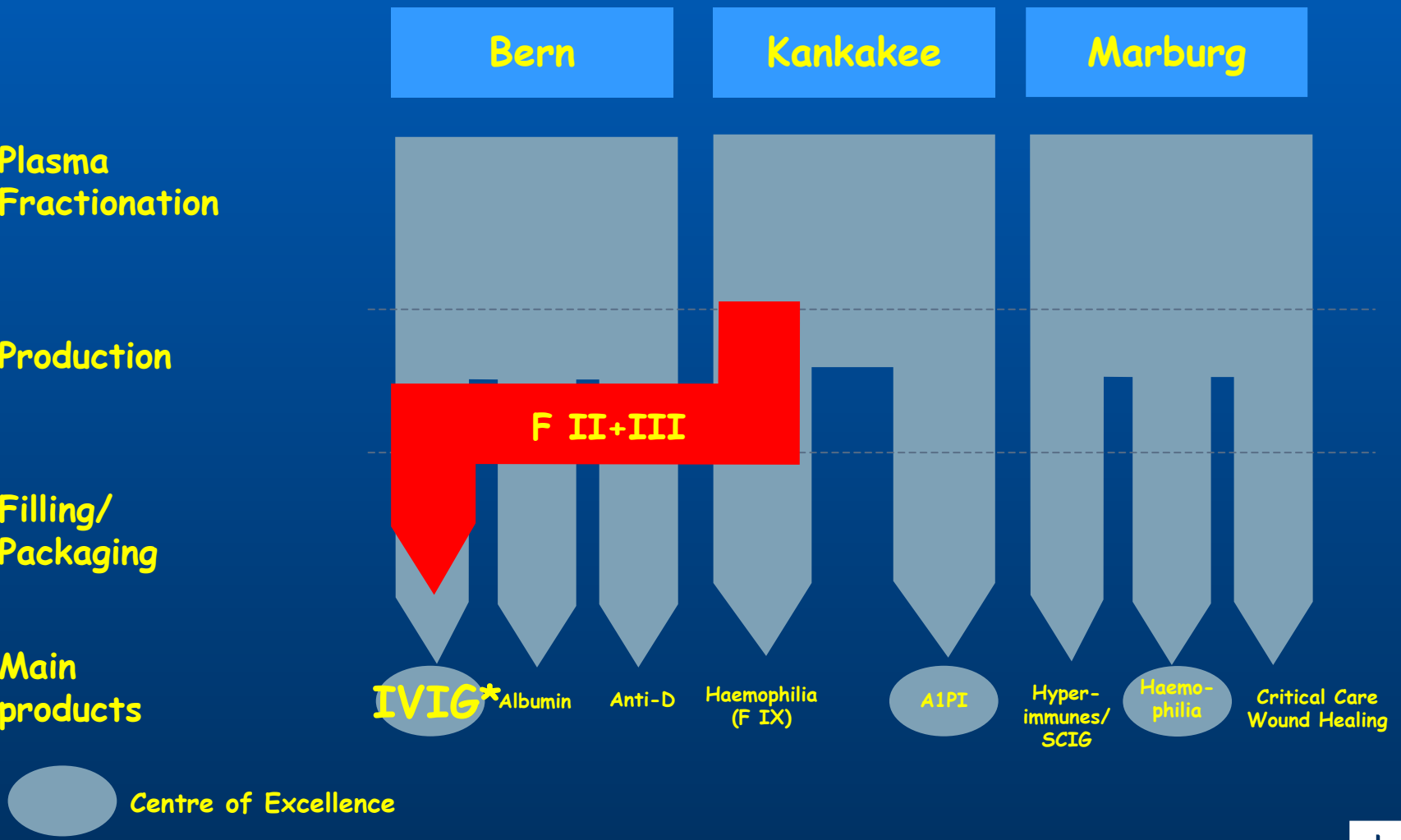


Broad portfolio of products - Global Sales Reach

Benefits of Integration for Key Products

IVIG	• Gammar P • Gamma Venin • Venimmune	→	• Carimune / Sandoglobin
Anti-D	• Rhesogam	→	• Rhophylac
Critical Care	• Albuminar	→	• ZLB-Albumin / Human Albumin

Operational Centres of Excellence



Increased IVIG output from Bern

- Current supply of IVIG will be met by improved manufacturing efficiencies.
- **FDA requirements for processing Kankakee Fr II+III paste now met and manufacturing commenced.**

Major synergy project completed

R&D portfolio December 2004: Plasma Products

Immunoglobulins
Liquid IVIG products
Subcutaneous IG
Anti D for ITP

Wound Healing
Fibrin Sealant
(Beriplast reconstitution and delivery)

Coagulation factors
vonWillebrand's disease
(Haemate/Humate NexGen)
Anti-coagulant reversal
(Beriplex P, EU)

Protease inhibitors
C1 esterase inhibitor
(Berinert P for USA)
Alpha-1-PI

Other projects
rHDL process
Pathogen Safety

Strengthening Our IVIG Portfolio

Sandoglobulin ®

(Lyophilised, IV)

Sandoglobulin ® Liquid

(12%, IV)

Chromatographic

(10% IV)

Opening New Markets for IgG

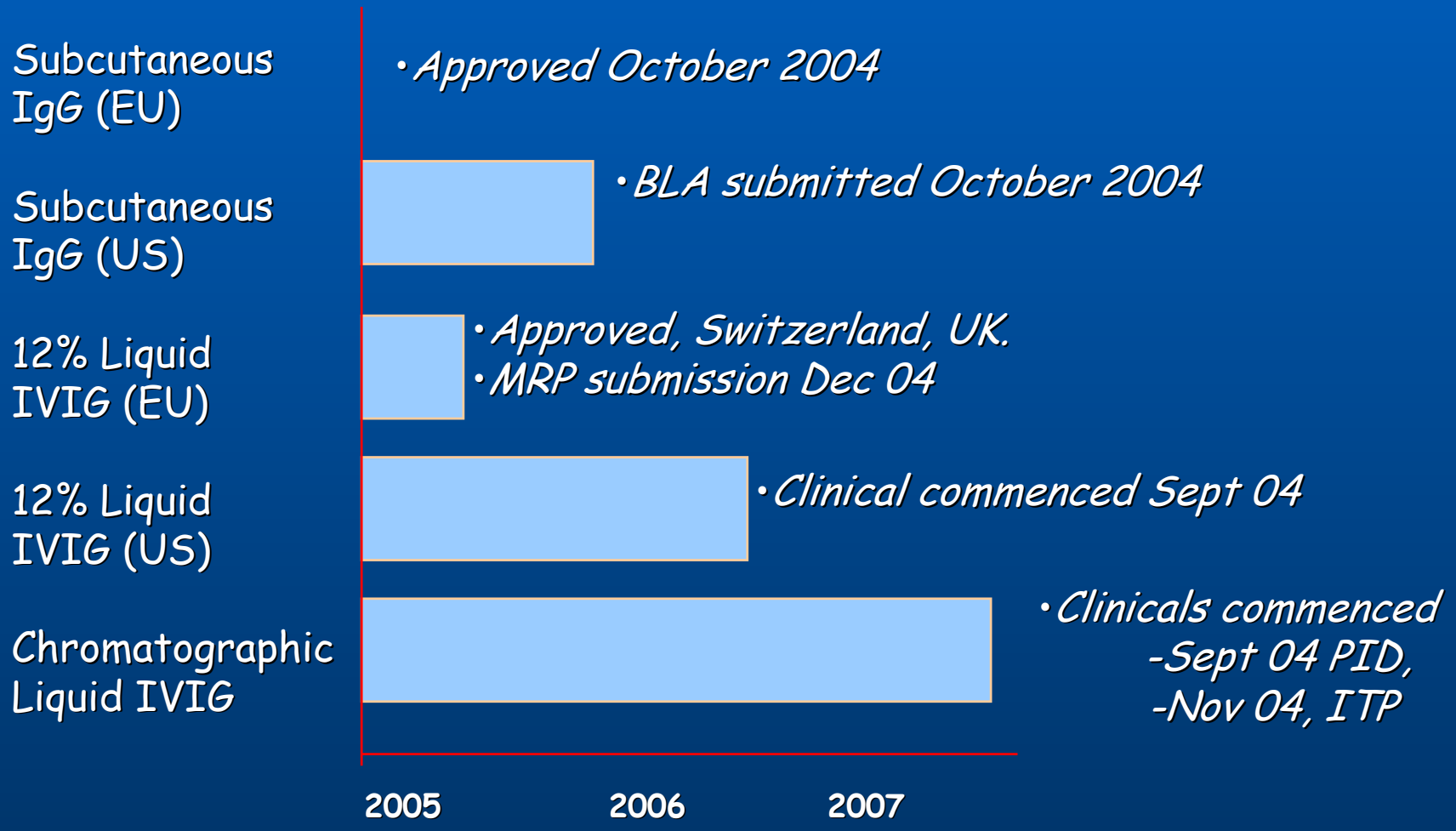
- Vivaglobin™
  - Subcutaneous IgG: 16%
  - For treatment of immunodeficiency
  - Well tolerated
  - Home therapy/self infusion (weekly)
- Improving diagnosis of immunodeficiency
  - The Jeffrey Modell Diagnostic Center for Primary Immunodeficiencies at The Children's Hospital of Philadelphia

Chromatographic IVIG

State of the art quality with manufacturing efficiency

- In house Swiss and Australian technology
- Liquid, 10% ready to use
- Comprehensive pathogen safety data
- High yield and purity

IgG portfolio: Timelines and milestones



Neurology and Immunoglobulins

- Expansion of label claims
  - Applying for GBS indication in the USA
- Supporting education in emerging markets

IVIG in Neurological Diseases

- Exploring new indications

- Hemolytic disease of the newborn (HDN)
- High product purity allows for **IV or IM** administration
- Liquid product
- Yield over 3 times Rhesogam
- US approval received in February 2004
- Registration expanded to 16 EU countries in 2004

- ***Anti D for ITP submissions Q1 05***

HaemateP/Humate P : vWF-FVIII conc. Superior product features

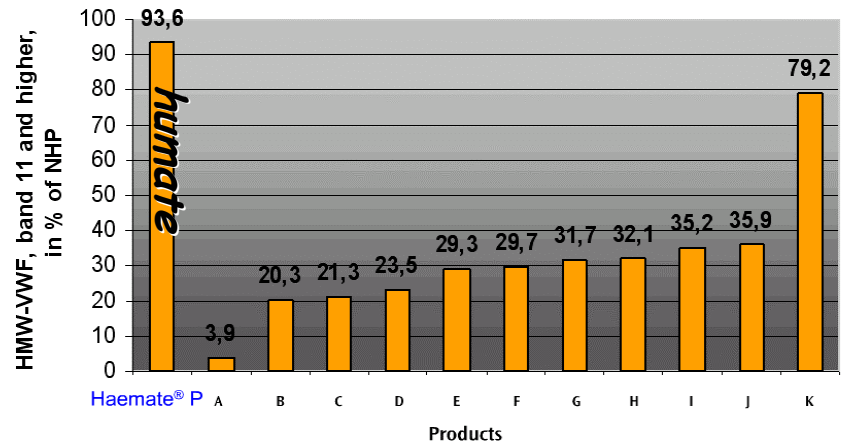
on Willebrand's Disease: 1-2% of population. Under diagnosed

onWillebrand factor: initiates formation of hemostatic plug , stabilises FVII

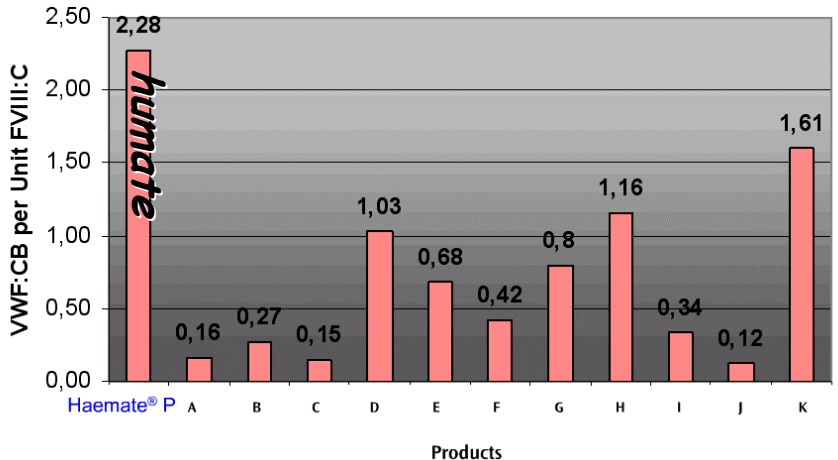
High MW multimers
- *important for efficacy*

High collagen binding
- *a measure of vWF activity*

Content of HMW-VWF – NHP=100%



VWF:CB per Unit FVIII:C



Humate P/Haemate P NexGen
Improved formulation, use in surgery

Improved formulation

- 2 fold reduction in volume
- Increase convenience
- Retains high MW multimers and activity
- To be introduced in 2005…

- **Developing use in surgery (US)**

Market leader in vWF concentrate

Wound Healing- Fibrin sealant:

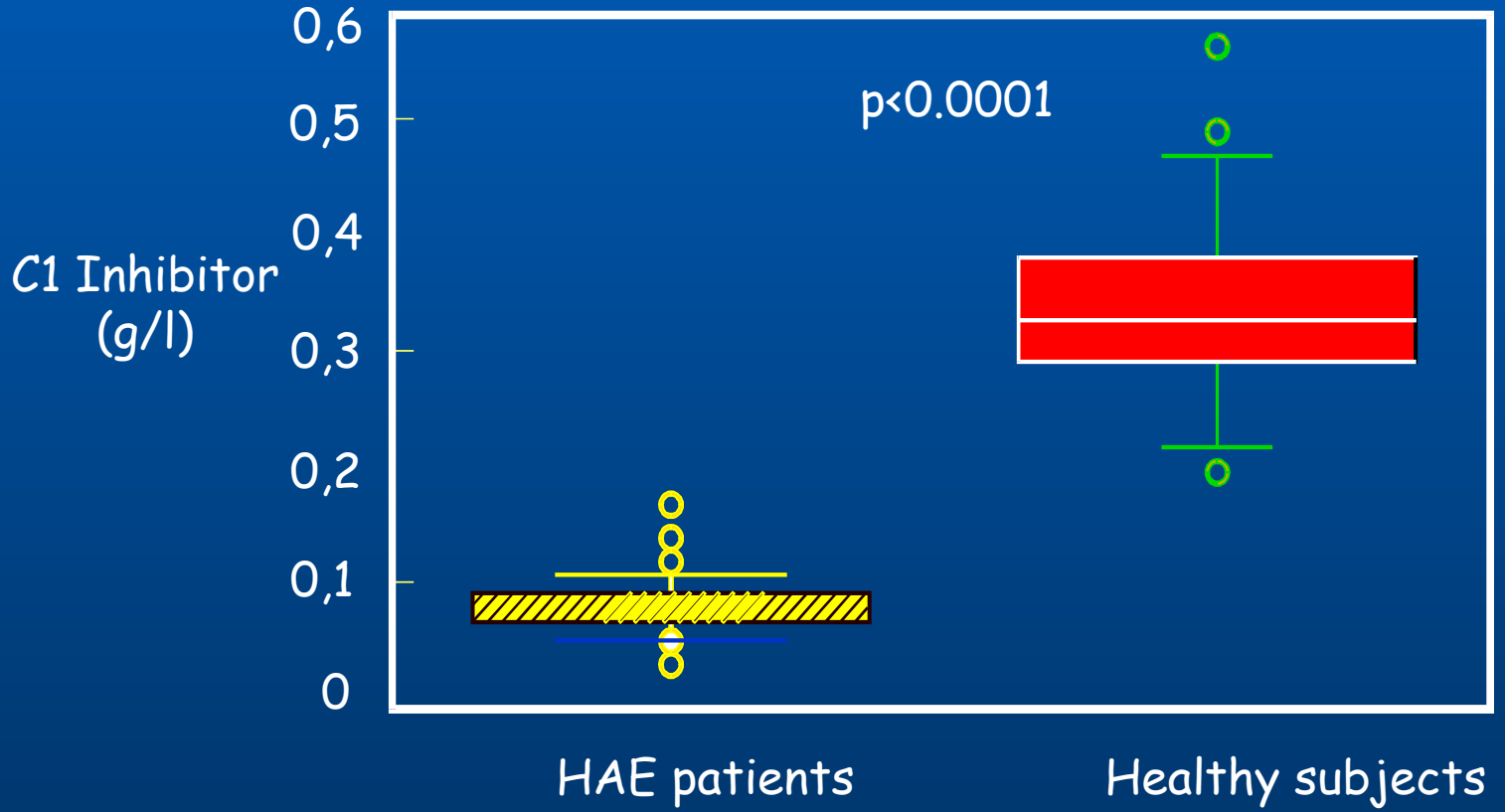
For sealing leakages associated with surgical procedures

- Beriplast Combiset (fibrin sealant)
  - Lyophilised fibrinogen and thrombin
  - Combiset registered in EU and Japan
  - Key market is Japan
  - Improved reconstitution and delivery systems to be introduced in 2005

TachoComb® (Nycomed): Another mode of delivery

- TachoComb® (Collagen/fibrinogen/thrombin)
  - Sealing and prevention of fistulae
  - Sealing and prevention of air leaks in pulmonary surgery
  - Anastomosis protection
  - Sealing of perforations of the eardrum
  - Sealing of dura mater defects
  - Manufactured using ZLB Behring fibrinogen and thrombin
  - Distributed by ZLB Behring in Japan

C1 Inhibitor Deficiency

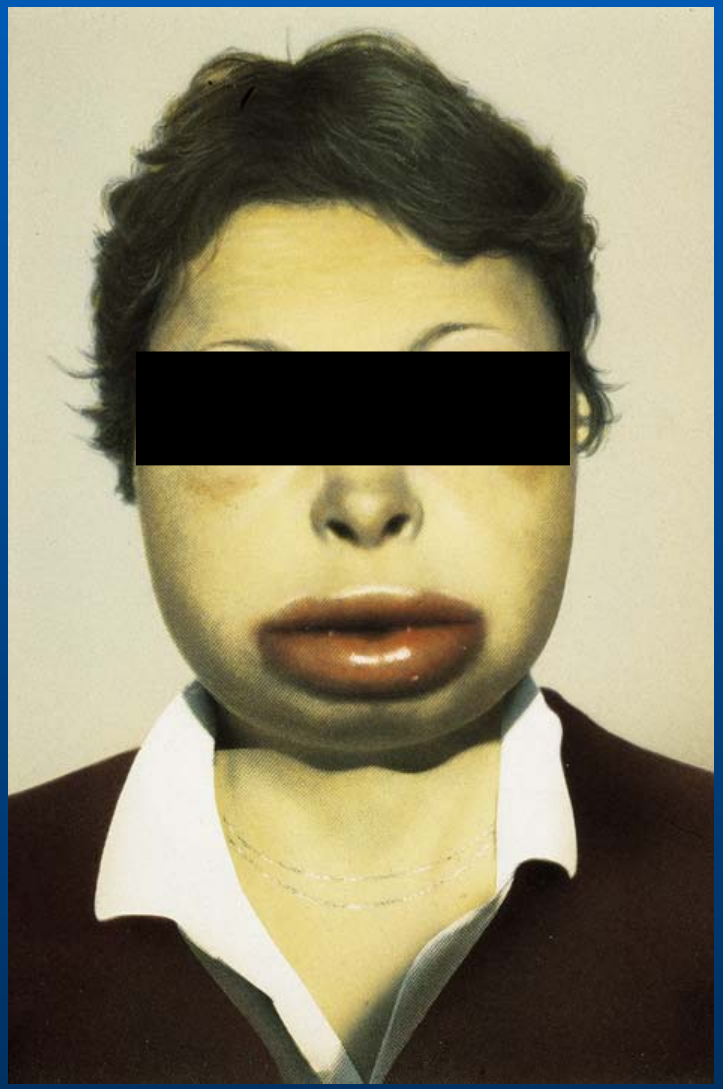


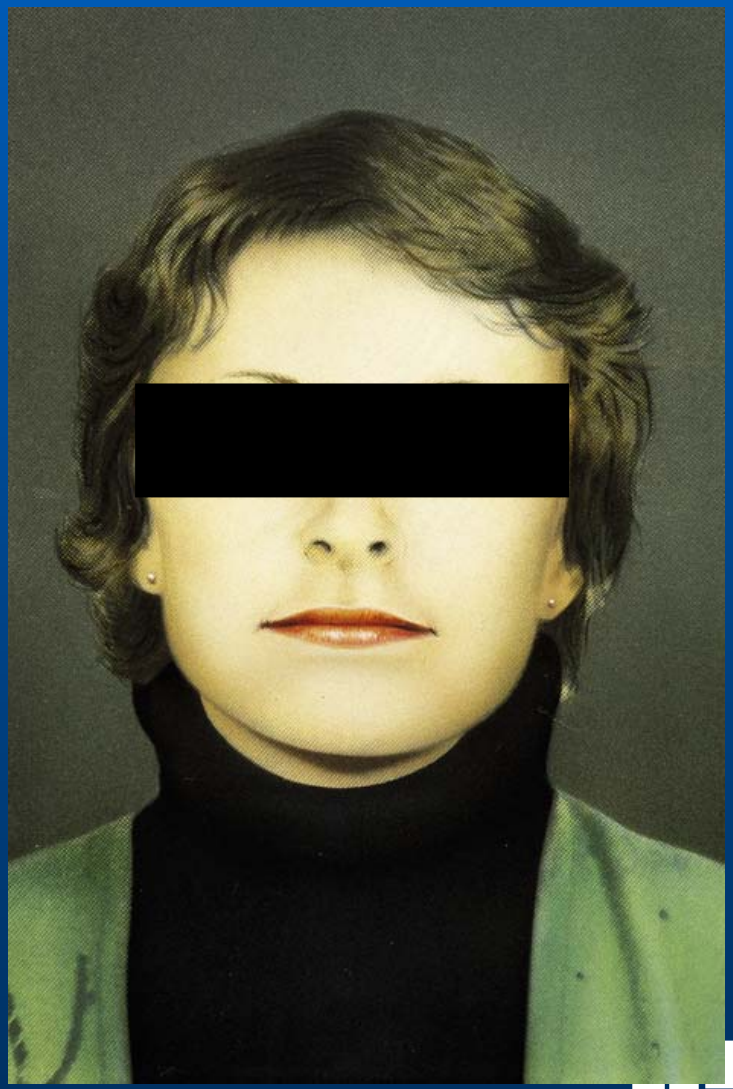
Nielsen, J of Int Med 1996; 239: 119

Heriditary Angioedema

Incidence: 1 in 50,000.

Ave: 1 attack per month. Can be fatal.





Berinert P (C1 esterase inhibitor)

- Registered in Germany, Japan, Austria, Hungary and Switzerland, Argentina
- Clinical trial design for treatment of acute episodes under development
- Competition
  - Dyax/Genzyme: kallikrein inhibitor
  - Jerini: bradykinin receptor antagonist
  - Pharming: transgenic C1 esterase inhibitor
- Competitive advantage of Berinert P: half life and multifactorial action.

Alpha-1-proteinase inhibitor deficiency

Incidence: 1: 6000 (under diagnosed)
Dose: 60mg per kg once per week

- Deficiency leads to emphysema later in life with significant lifestyle impacts
- ZLB Behring has recently entered the US market

Zemaira™
alpha$_1$-proteinase inhibitor (Human)
Expect Purity. Expect Convenience.

Zemaira: Superior Profile

- Zemaira: Purity, rapid reconstitution, low volume.
- Market base growing
- Phase IV trials planned in 2005
- Validation of new facility in Kankakee near completion with FDA approval expected second half 2005

A track record of safe plasma products and reputation for leading safety standards

Virus Safety

- Viral Inactivation processes dealing with both enveloped and non-enveloped viruses
  - Pasteurisation
  - Nanofiltration
  - SD technology
  - Low pH treatment
- Emerging viruses (e.g West Nile, SARS) inactivated by these processes.

A track record of safe plasma products and reputation for leading safety standards

Prion Safety

- State of the art in-house technology for measuring capability of processes to eliminate prions should they be present in plasma.
- First company to get FDA approved label claim for capability of process to eliminate prions

Complementary laboratories maintaining state of the art virology and prion technologies.

Plasma Products Portfolio Summary

- Key R&D integration tasks completed and forecast savings delivered
- The major manufacturing synergy project completed
- Key R&D milestones for ongoing programs met
- New initiatives underway

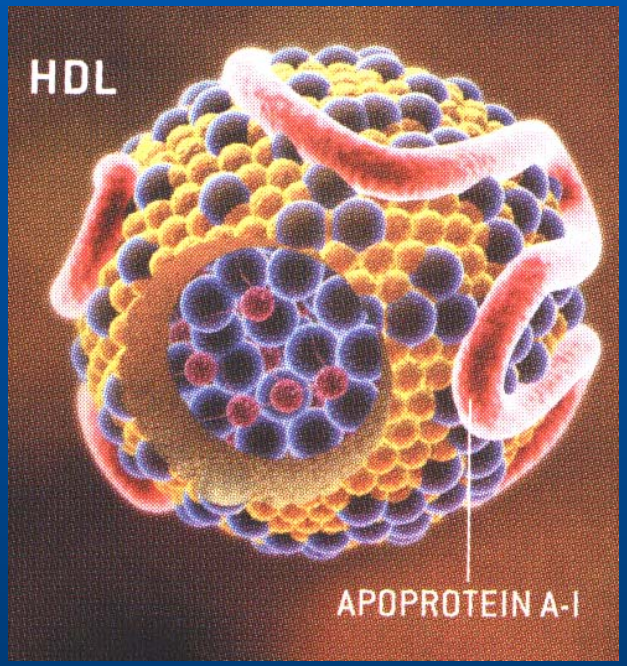
rHDL - Two Major Clinical Development Opportunities

Dr. Russell Basser

Global Clinical Director, New Product Development

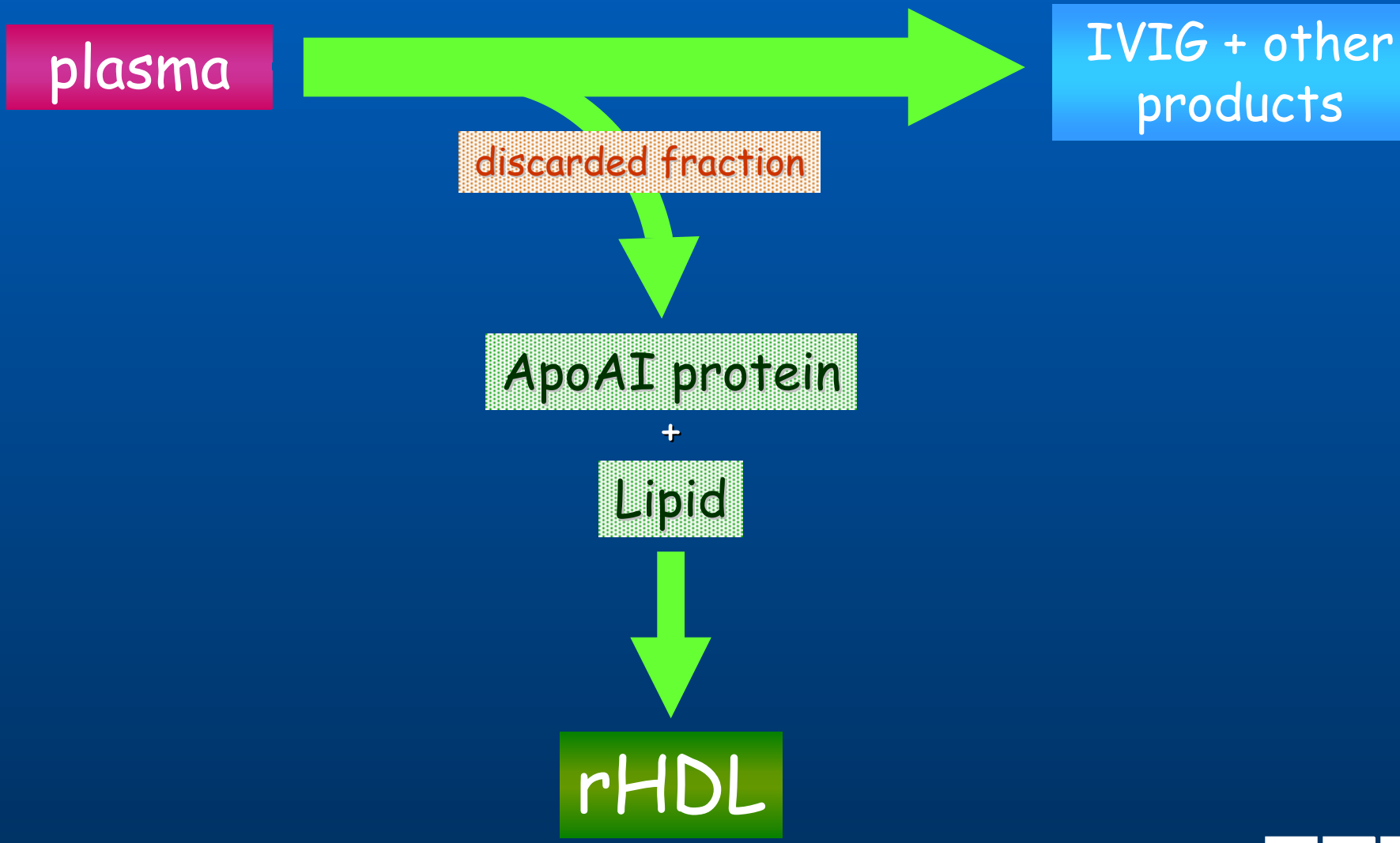
rHDL = Reconstituted high-density lipoprotein

HDL =
"good cholesterol"



rHDL =
a synthesized lipoprotein particle *chemically* and *biologically* resembling native HDL

Manufactured from discarded fraction of plasma



rHDL is safe & biologically active in humans

- Clinical trials in over 150 people
- Very well tolerated
- No serious or unpredicted side-effects
- Biological activity demonstrated

rHDL is a potent biological compound

- Extensive scientific work shows rHDL is active
  - anti-inflammatory
  - sucks cholesterol from vessel walls ("reverse cholesterol transport")
  - increases blood flow (vasodilator)
  - anti-oxidant
  - blood thinning (anticoagulant)

rHDL FOR ACUTE ISCHEMIC STROKE

PROGRESS WITH rHDL FOR STROKE

- Preclinical stroke work progressing
  - publication of Italian research results
  - Australian paper submitted
- Trial in stroke patients commenced Nov 04
  - safety and pharmacology
- Preparing for phase 2 study
  - effect of rHDL on size of stroke (by Magnetic Resonance scan)

rHDL FOR ACUTE CORONARY SYNDROME (ACS)

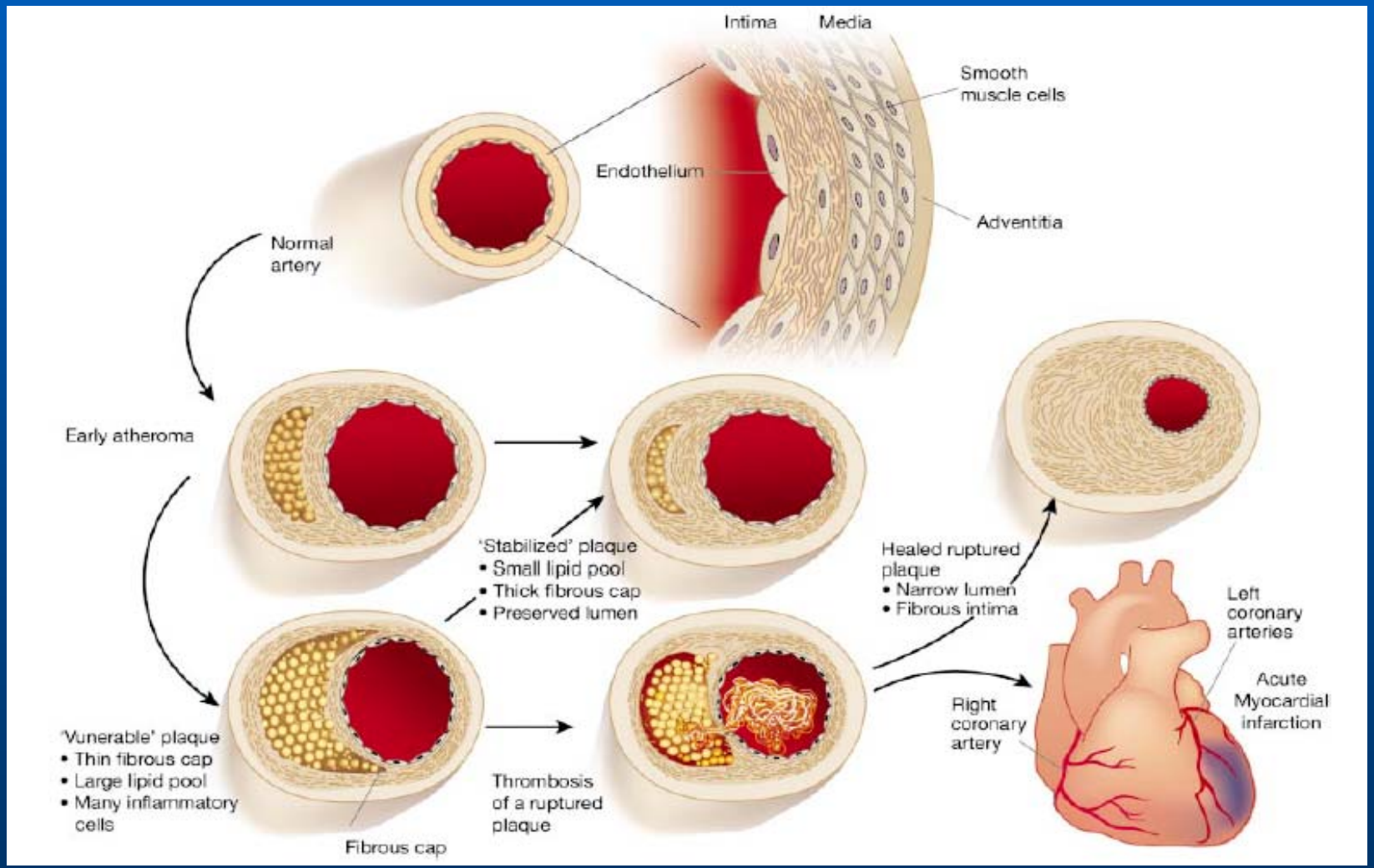
What is ACS?

- Myocardial infarction & unstable angina
- ~ 1.7M clinical episodes per yr in USA
- "Vulnerable patient"
  - generalised process in all coronary blood vessels
  - risk of a further clinical event despite current treatment (ie new infarction, medical intervention, surgery, death)
  - 10+% at 1yr, 15-20% at 2yrs

What happens in ACS?

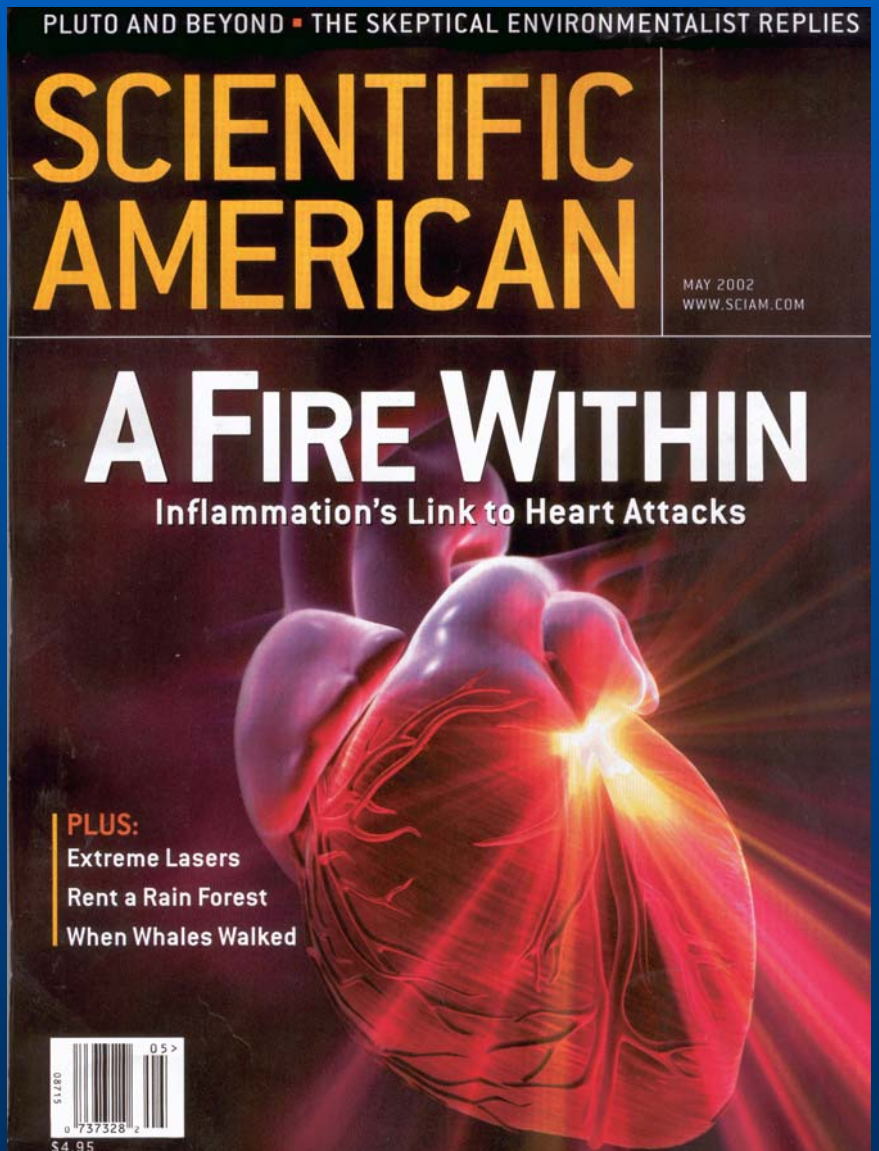
- Underlying problem is atherosclerosis
  - hardening and narrowing of the coronary arteries
  - starts from childhood
  - related to genes, environment, various medical conditions
- ACS occurs when a clot forms on ruptured segment of *unstable* atheroma (plaque)
  - blocks blood supply to area of heart muscle
  - results in chest pain with or without permanent damage

ACS: What's happening in the blood vessel?



Libby, Nature 2002

Inflammation is important in atheroma & ACS



Current treatment of ACS

- Treatments aimed at
  - maintaining blood flow in the affected blood vessel
  - limiting damage to heart
  - reducing the chance of further clot formation
  - delaying further progression (growth) of plaque

  - multiple drugs
    - aspirin, beta blocker, ACE inhibitor, statin
  - early procedure to look at plumbing (blood vessels)
    - keep open with stent (metal mesh)

Why is CSL interested in ACS?

- Information in animals & humans that rHDL has properties that are beneficial
  - reverse cholesterol transport
  - anti-inflammatory
  - anti-oxidant
  - calms chronically irritated endothelial (lining) cells
- Intellectual property, product supply and formulation strengths

The concept of rHDL for ACS

- infusion of rHDL provides rapid stabilisation of plaque
  - rapid removal of fat from blood vessel
  - rapid reduction in inflammation of the coronary arteries

➔ *rHDL will take the blood vessels back in time to a more stable and less aggravated state*

➔ *much less chance of further clinical problems*

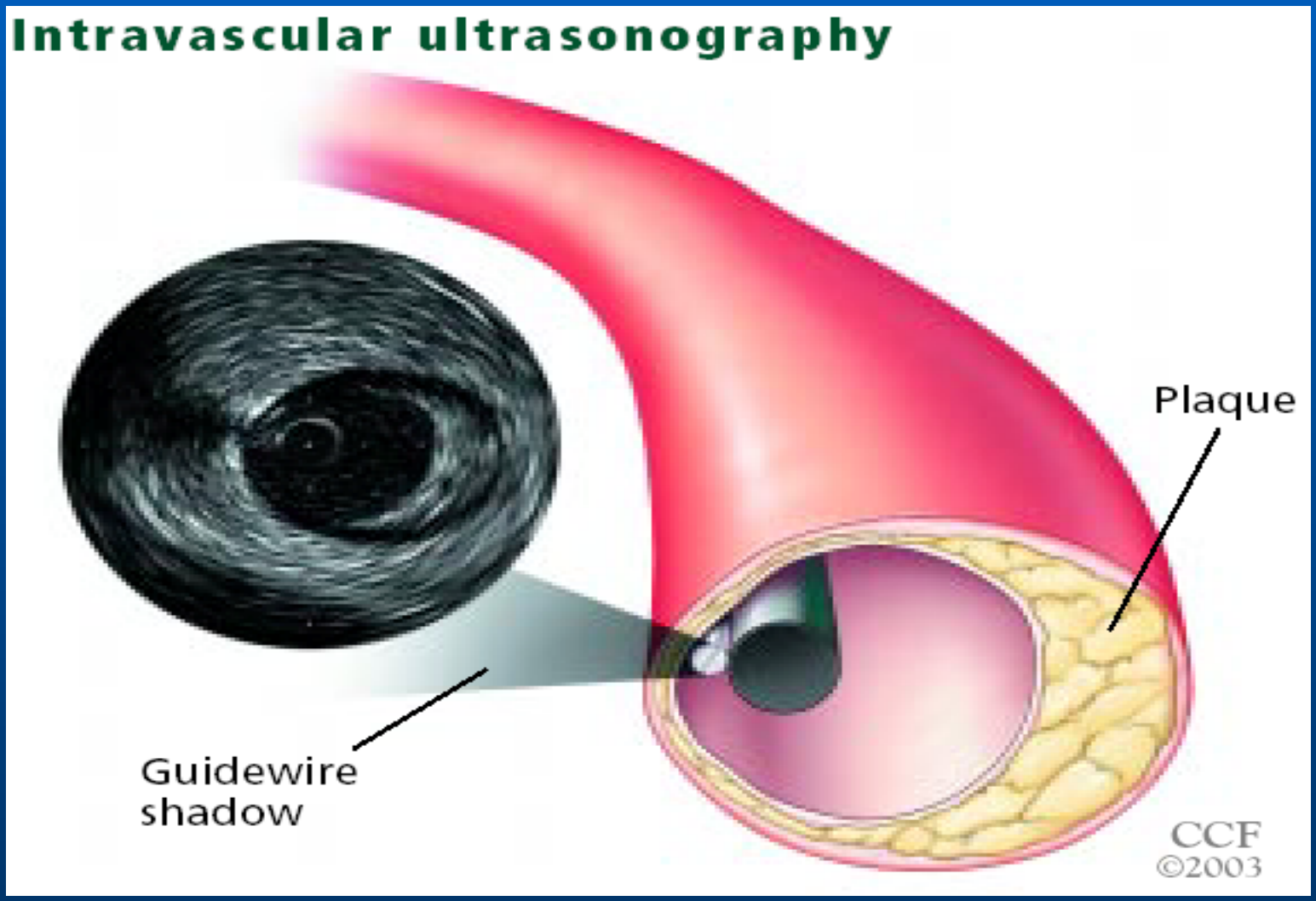
Product Concept to be Tested in Canadian Centre

- New diagnostic technology: able to conduct a Phase 2 clinical study
- Identified high quality cardiology group in Canada

High Quality Clinical Trial Opportunity

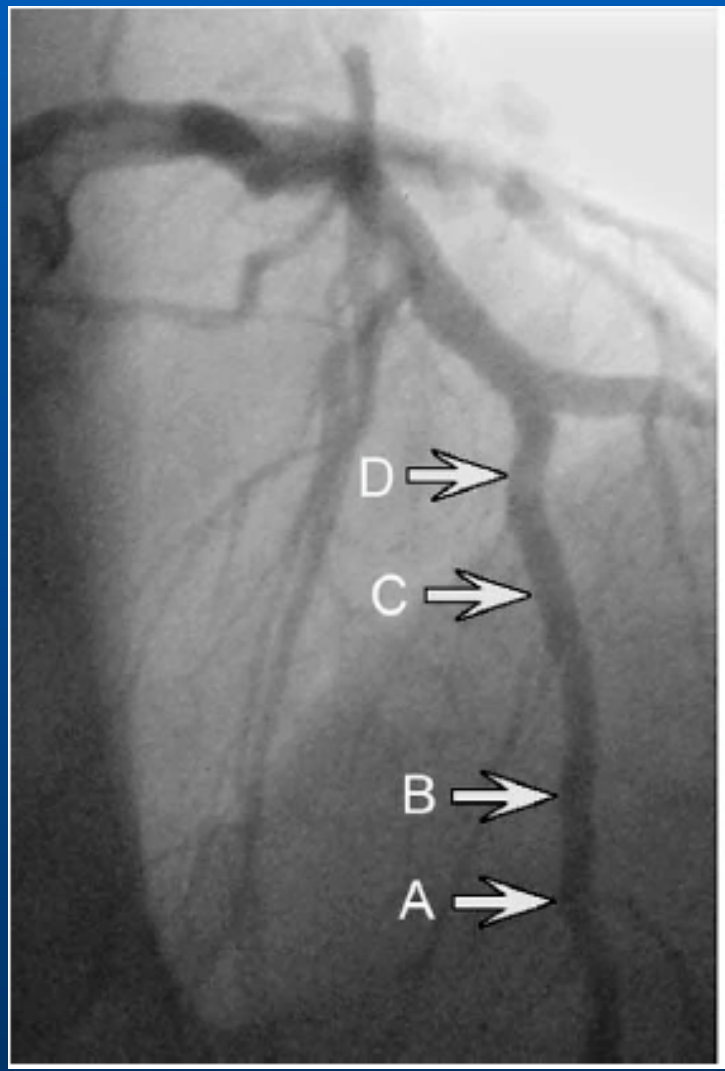
- Study based on intravascular ultrasound (IVUS) measure of plaque and blood vessel wall thickness
- Montreal Heart Institute (MHI)
  - Dr Jean-Claude Tardif is Director of Research
  - one of two state-of-art IVUS groups
  - network of cardiology investigators in Canada
  - high quality clinical trial infrastructure

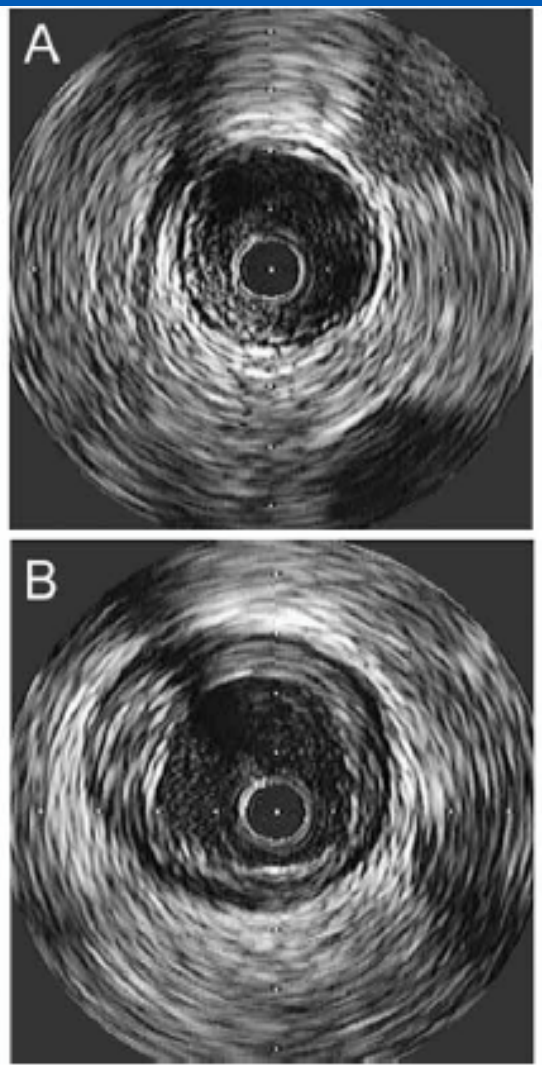
What is IVUS?

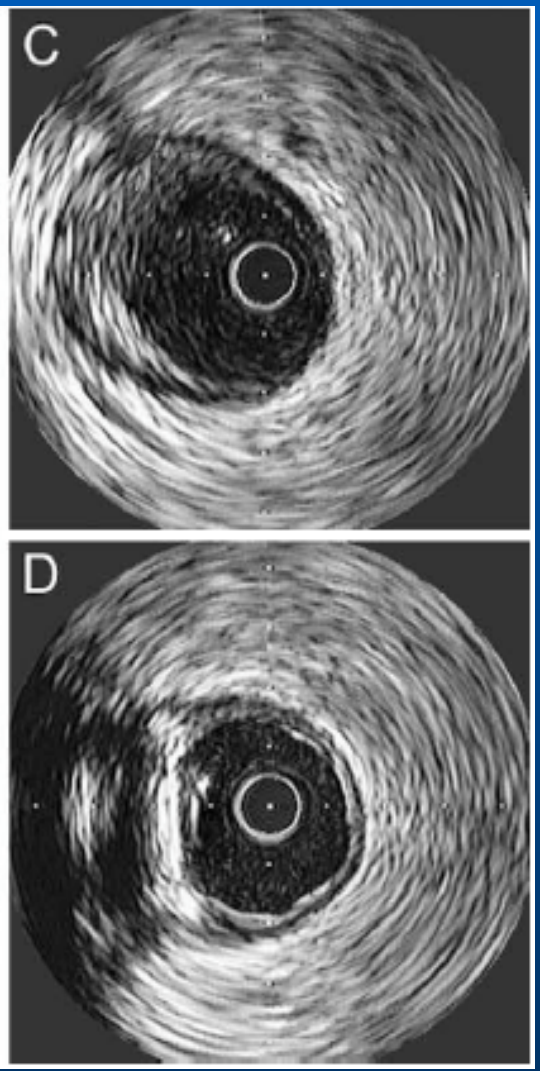


Schoenhagen et al, Clev Clin J Med 2003

IVUS shows details otherwise missed







Nissen, Am J Cardiol 2002

What might we expect to find?

- shrinkage of plaque
- reduction in inflammation

➔ *will give confidence that giving rHDL to patients with ACS is likely to provide clinical benefit*

Summary of rHDL projects

- Stroke indication progressing as planned
  - phase 2 trial planned to commence 2006
- ACS provides a complimentary opportunity
  - phase 2 trial to commence first half 2005
  - phase 2 results in 2006

Example of an Earlier Stage Opportunity

- Significant work by Australian researchers: Professor Doug Coster, Flinders Medical Centre
- Applying biotechnology to treating serious eye diseases

Topical Delivery of Recombinant Antibodies for Treating Eye Disease

- US Patent Issued
- Continuing to evaluate in preclinical experiments

R&D Highlights from 2004

- Merck HPV clinical trial progress
- ZLB Behring integration advanced with financial targets on track
- 2+3 paste registered in Bern
- Vivaglobin s.c. approval EU, US submitted
- First stroke patients treated and ACS indication for rHDL
- New Chlamydia ISCOMATRIX® collaboration with Aventis
- Topical delivery for eye disease patent issued