

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

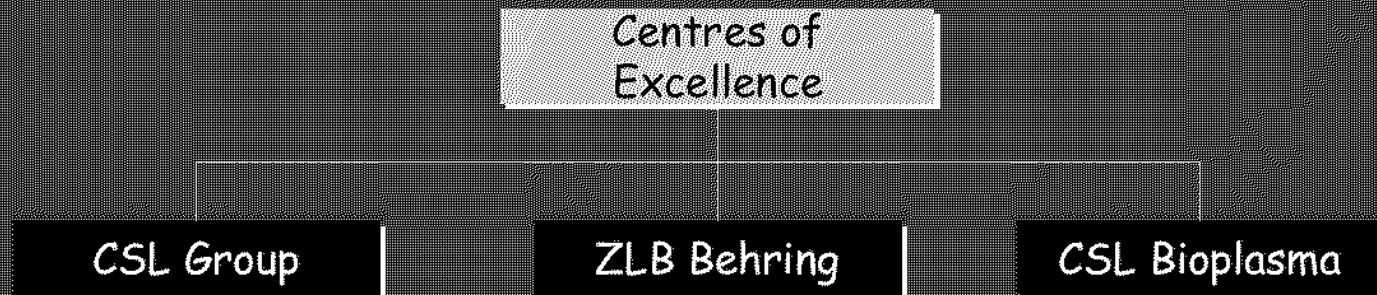
R&D - Investment Objectives

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



• 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

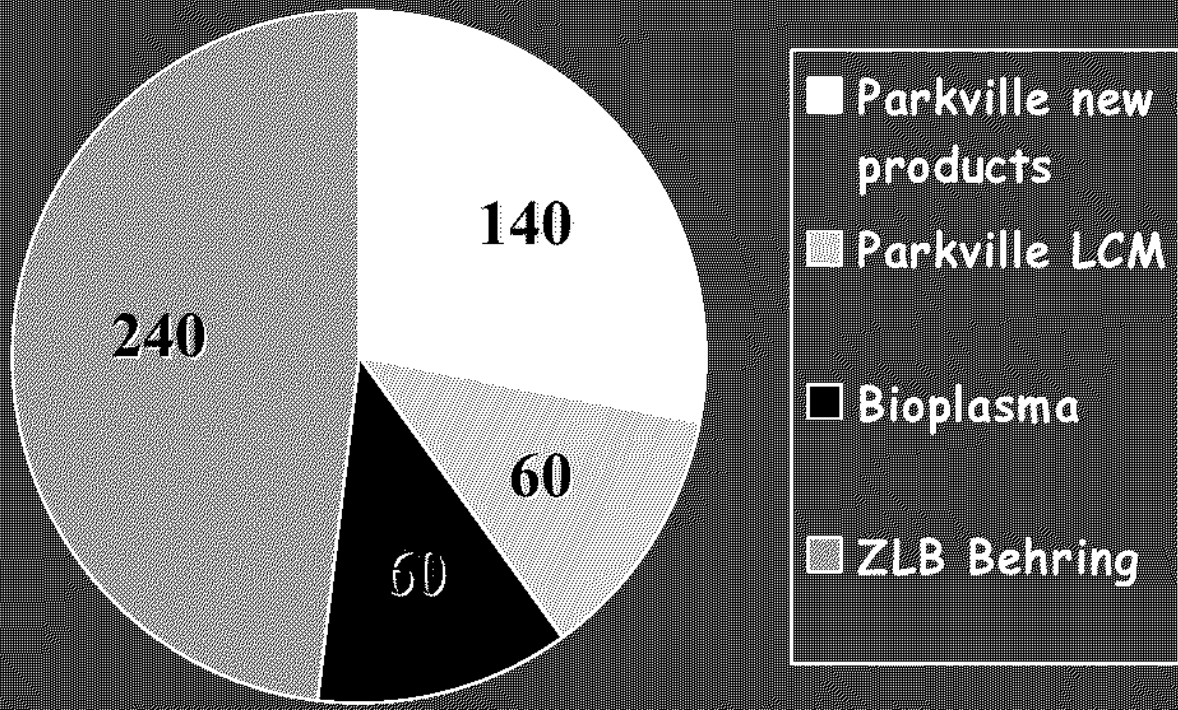
• Laboratories

- 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

PharmaPlan

Strategy & Investment

New
Opportunities

Project
Management

Project
Review

Commercial

Identification
Evaluation
Testing

Operations
Financial
Strategy

Performance

Analytical
Deal Making

R&D PORTFOLIO December 2004: Novel Protein Product Development

HPV Prophylaxis

Clinical Trials

- rHDL
 - Stroke
 - ACS
- HPV Therapy

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

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

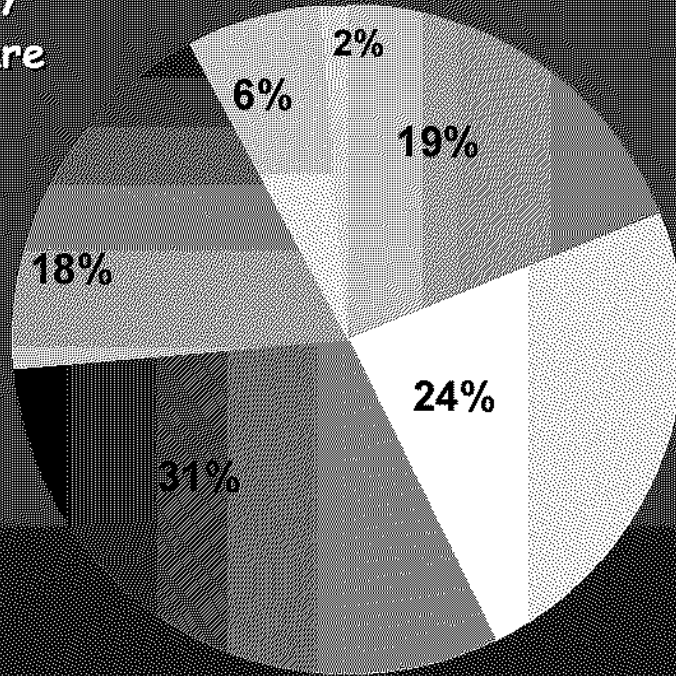
R&D Integration is Well Advanced

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

R&D Supports a Major Global Product Portfolio

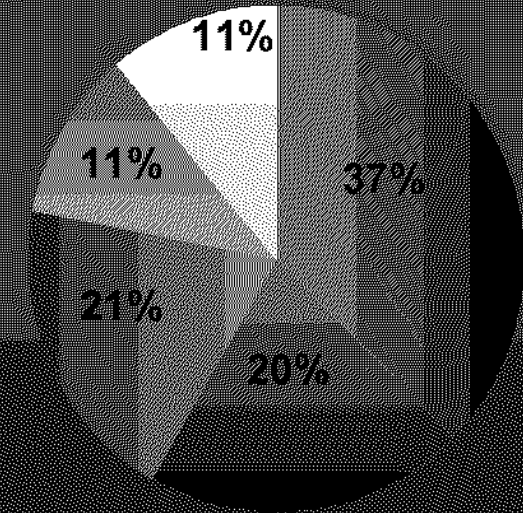
Per Therapeutic Category % Total Sales

- rFVIII
- Pd Coagulation
- Immunology
- Critical Care
- Wound
- Healing
- Other



Per Region % Total Sales

- North America
- Western Europe
- Central Europe
- Japan
- Intercontinental



Broad portfolio of products - Global Sales Reach

Benefits of Integration for Key Products

IVIG

- Gammar P
- Gamma Venin
- Venimmune



- Carimune / Sandoglobulin

Anti-D

- Rhesogam



- Rhophylac

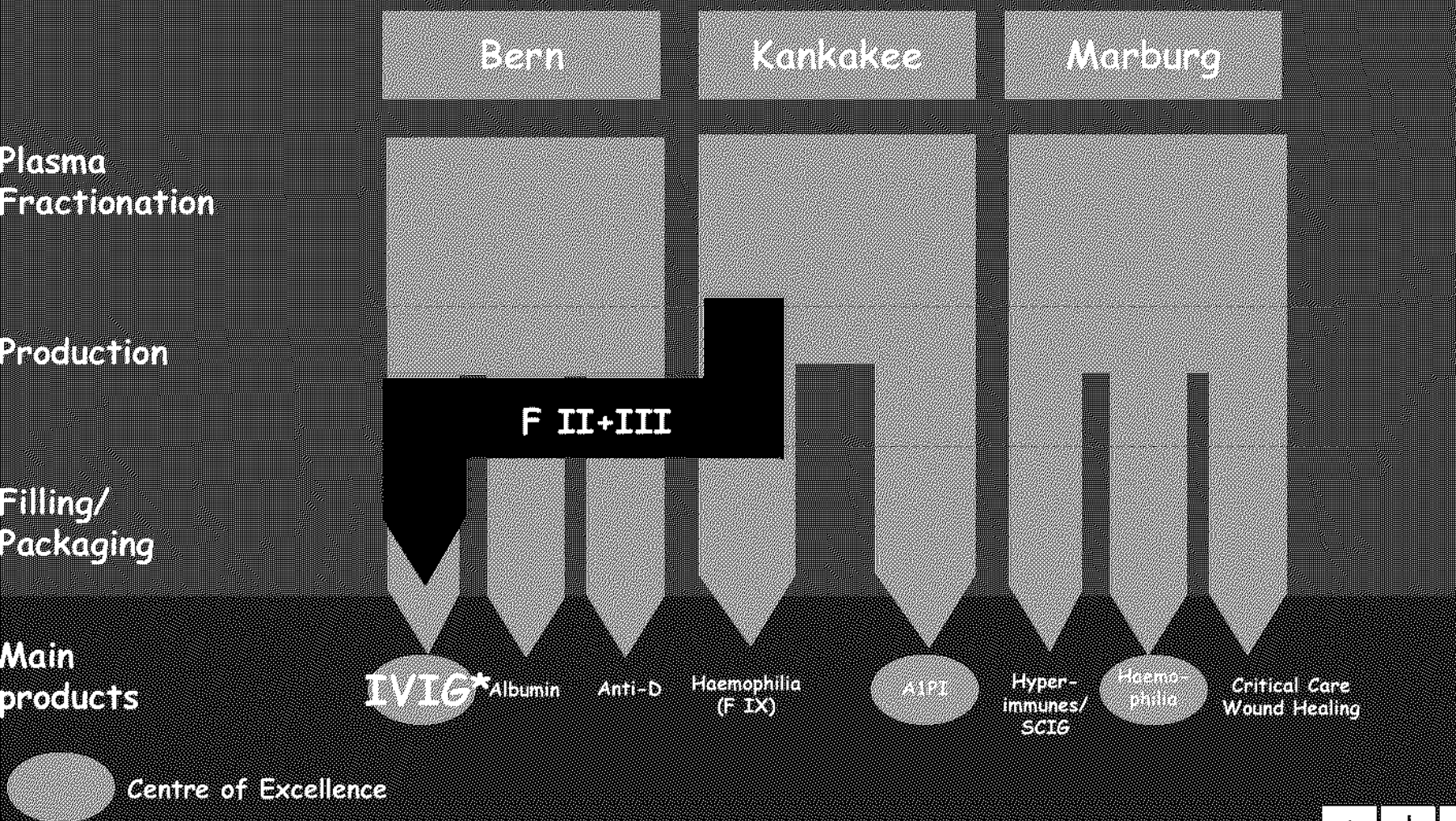
Critical Care

- 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

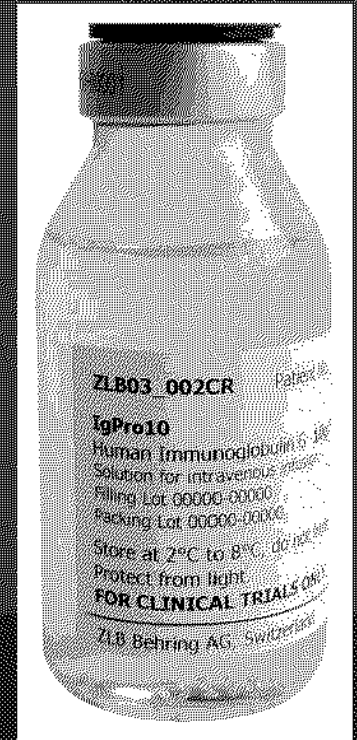
Strengthening Our IVIG Portfolio



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

Subcutaneous
IgG (EU)

• *Approved October 2004*

Subcutaneous
IgG (US)

• *BLA submitted October 2004*

12% Liquid
IVIG (EU)

• *Approved, Switzerland, UK.*
• *MRP submission Dec 04*

12% Liquid
IVIG (US)

• *Clinical commenced Sept 04*

Chromatographic
Liquid IVIG

• *Clinicals commenced*
- *Sept 04 PID,*
- *Nov 04, ITP*

2005

2006

2007

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



Rhophylac[®]

Rh₀(D) Immune Globulin
Intravenous (Human)

- 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

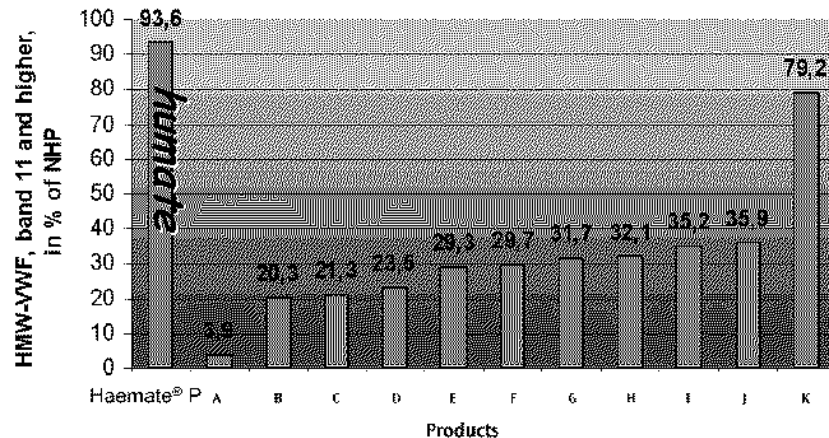
on Willebrand's Disease: 1-2% of population. Under diagnosed

on Willebrand factor: initiates formation of hemostatic plug , stabilises FVIII

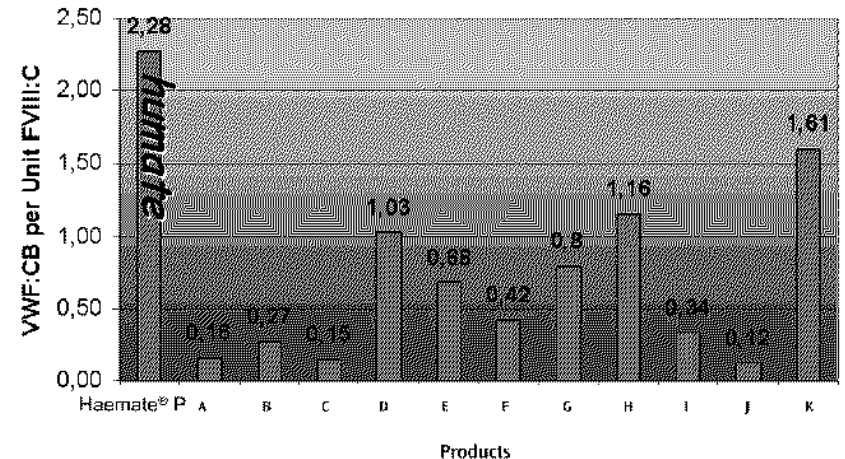
High MW multimers
· *important for efficacy*

· *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...

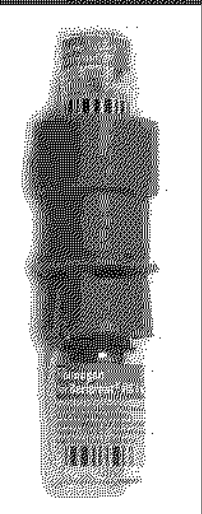
- Developing use in surgery (US)

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

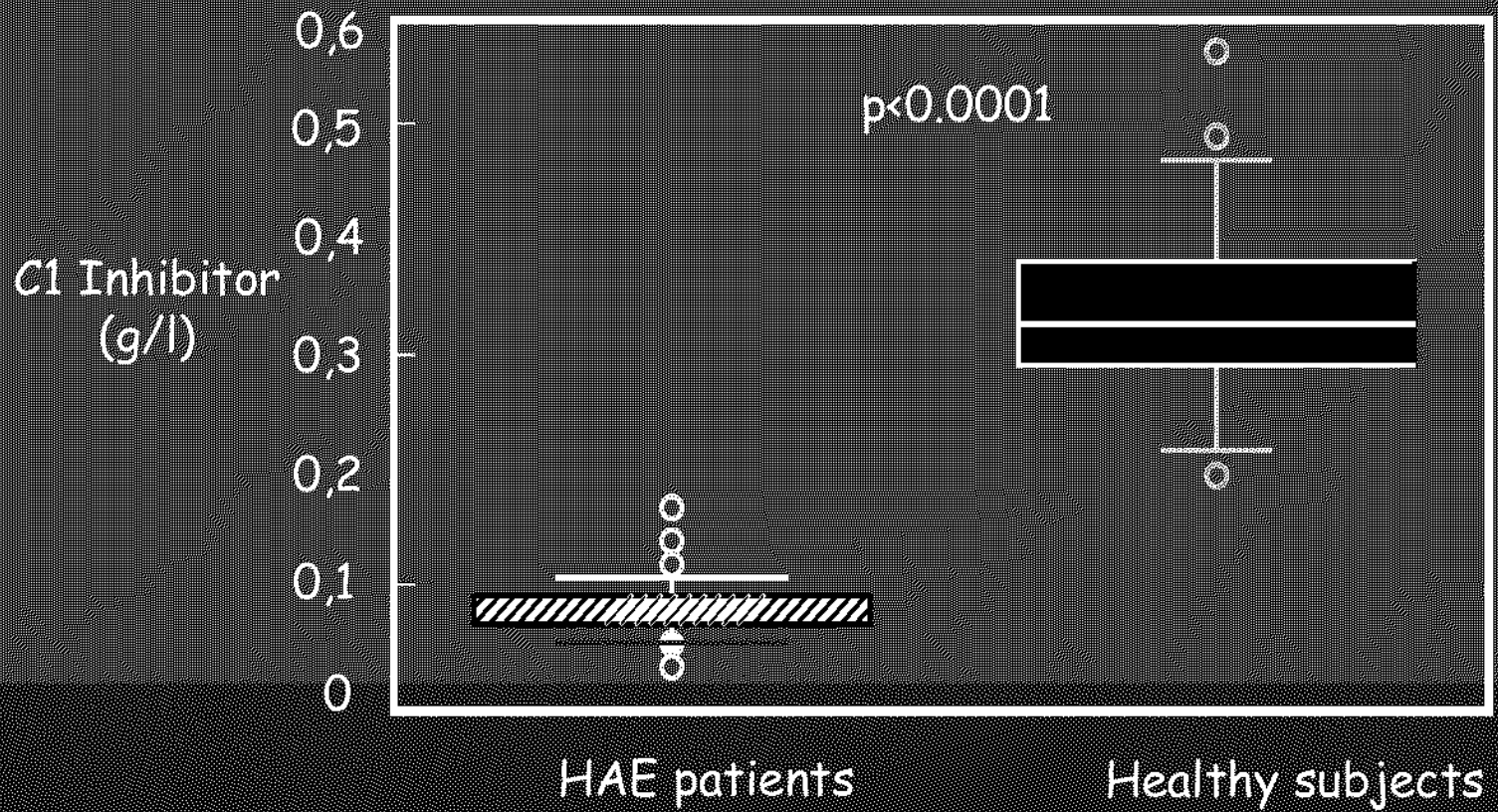


TachoComb® (Nycomed): Another mode of delivery

- 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



Hereditary Angioedema

Incidence: 1 in 50,000.

Ave: 1 attack per month. Can be fatal.



Beriner 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 Beriner 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™**
alpha₁-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

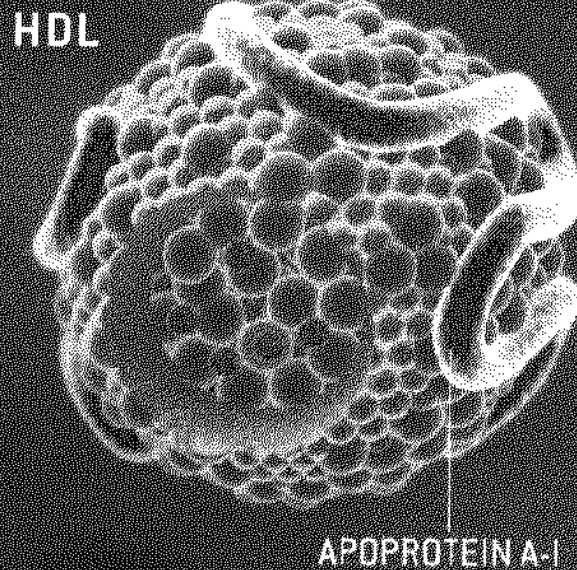
- Key R&D integration tasks completed and forecast savings delivered
- The major manufacturing synergy project completed
- Key R&D milestones for ongoing programs met
- New initiatives underway

rHDL - Two Major Clinical Development Opportunities

Dr. Russell Basser
Global Clinical Director, New
Product Development

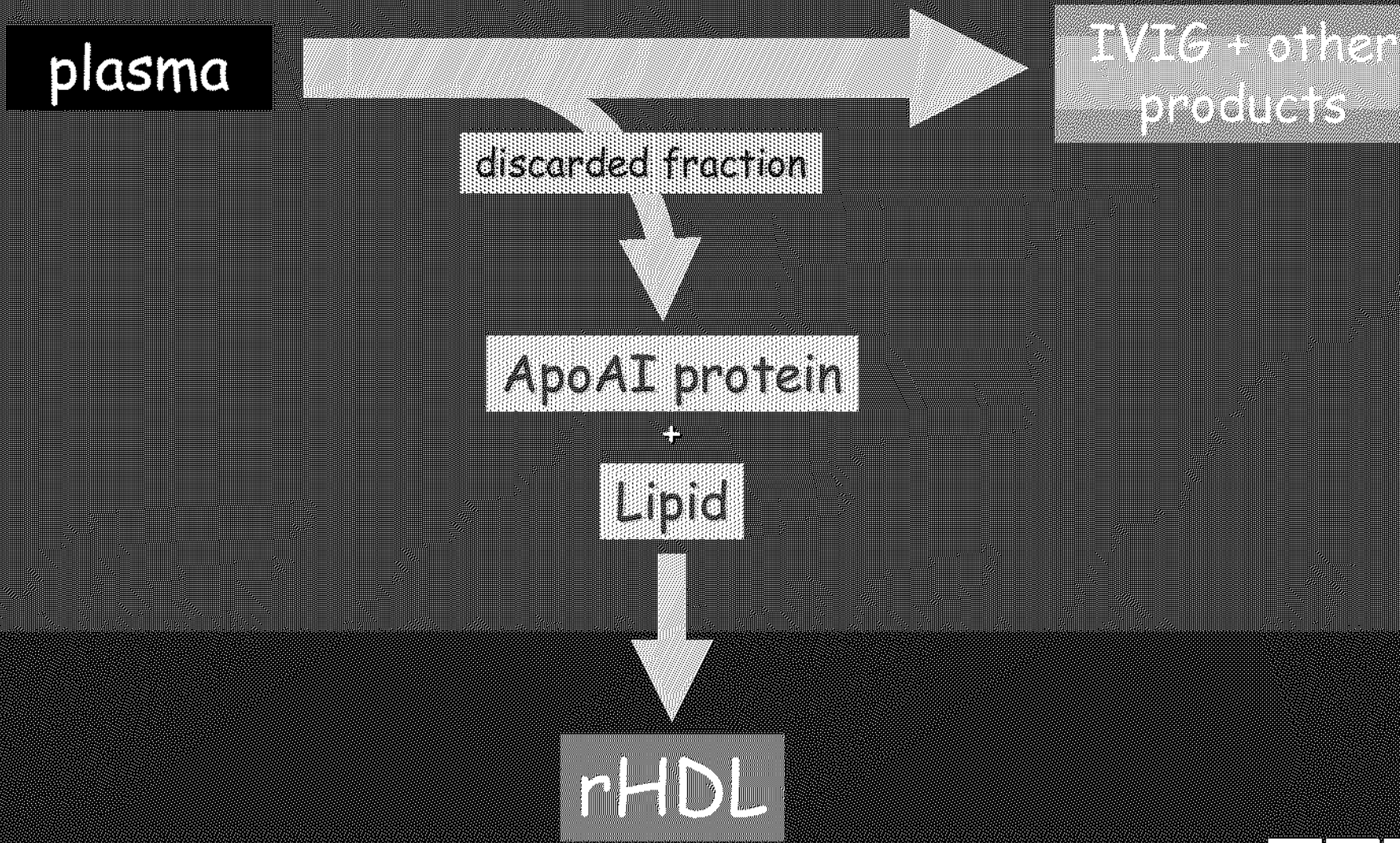
rHDL = Reconstituted high-density lipoprotein

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)

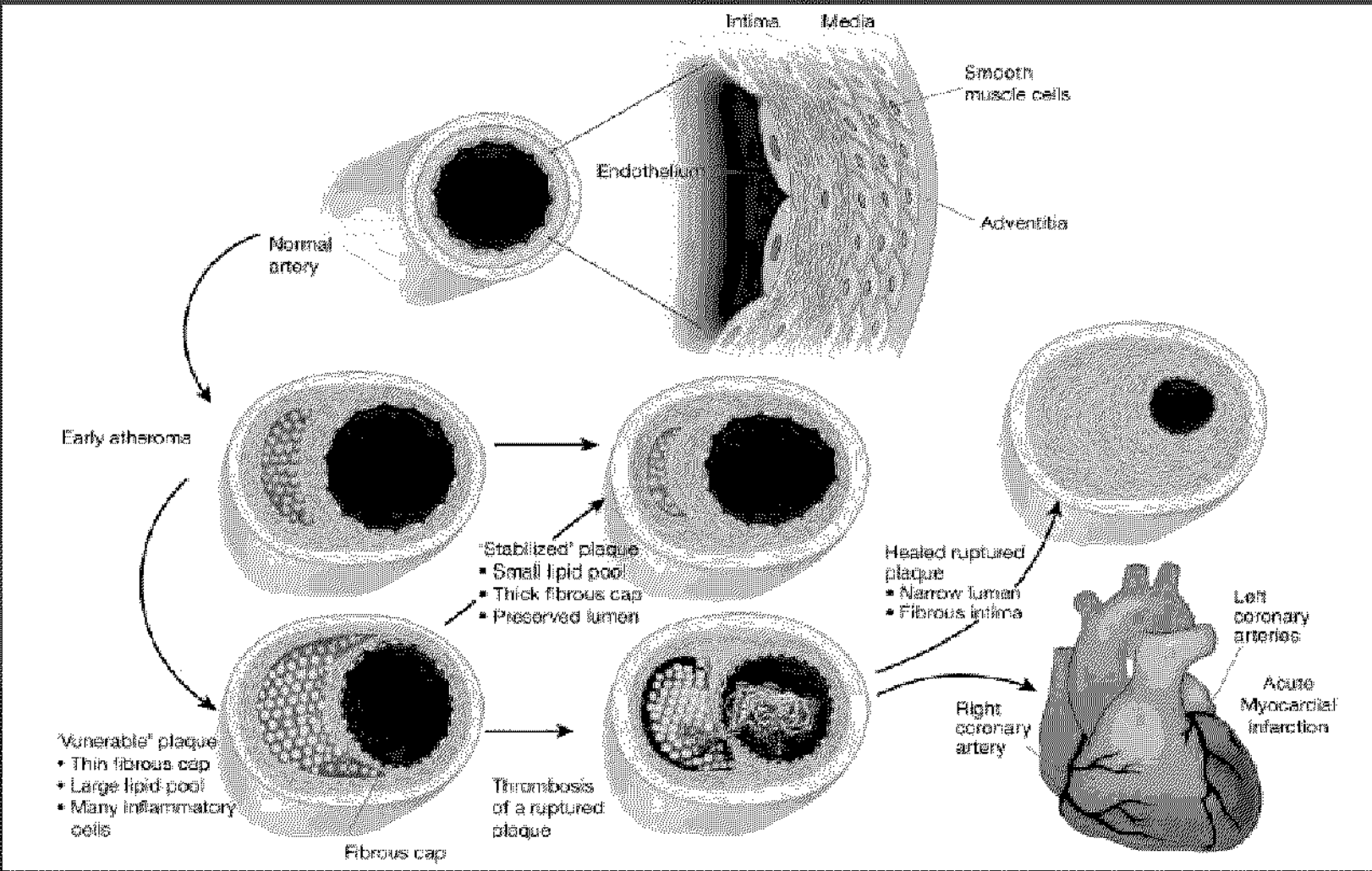
What is ACS?

- 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

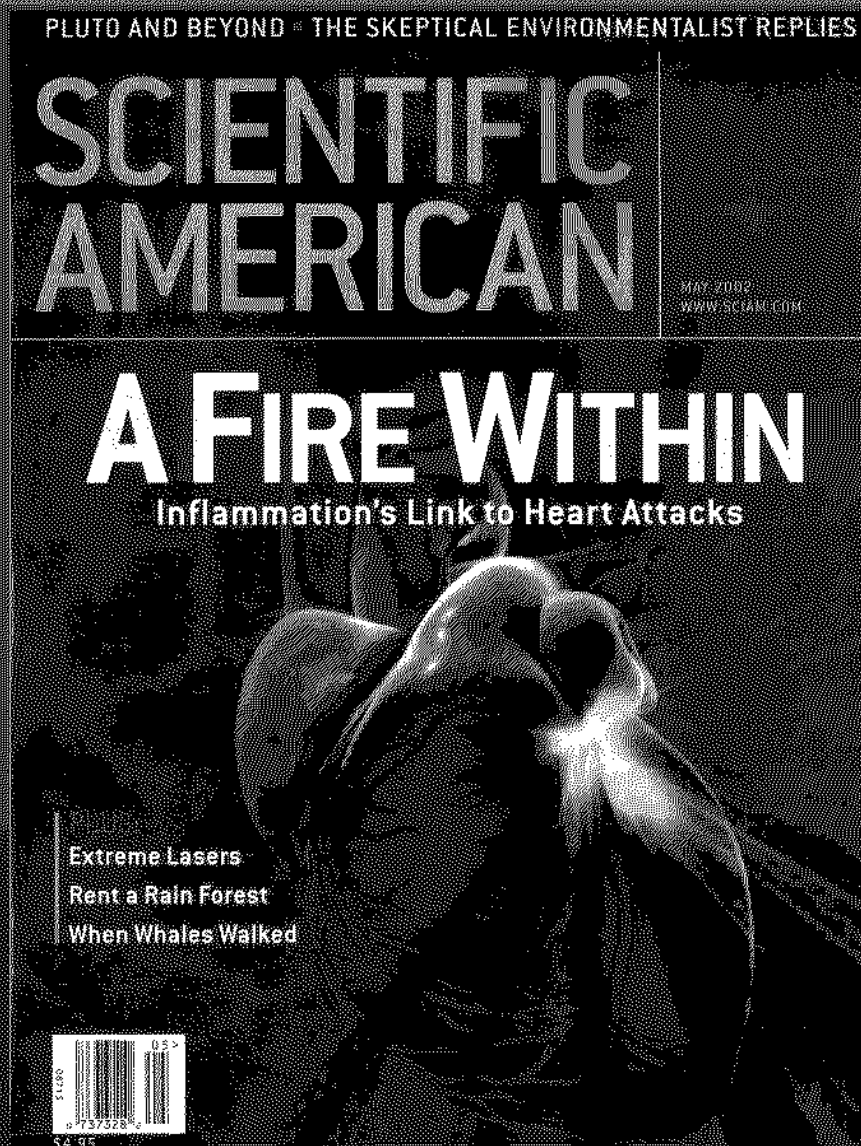
What happens in ACS?

- 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?



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

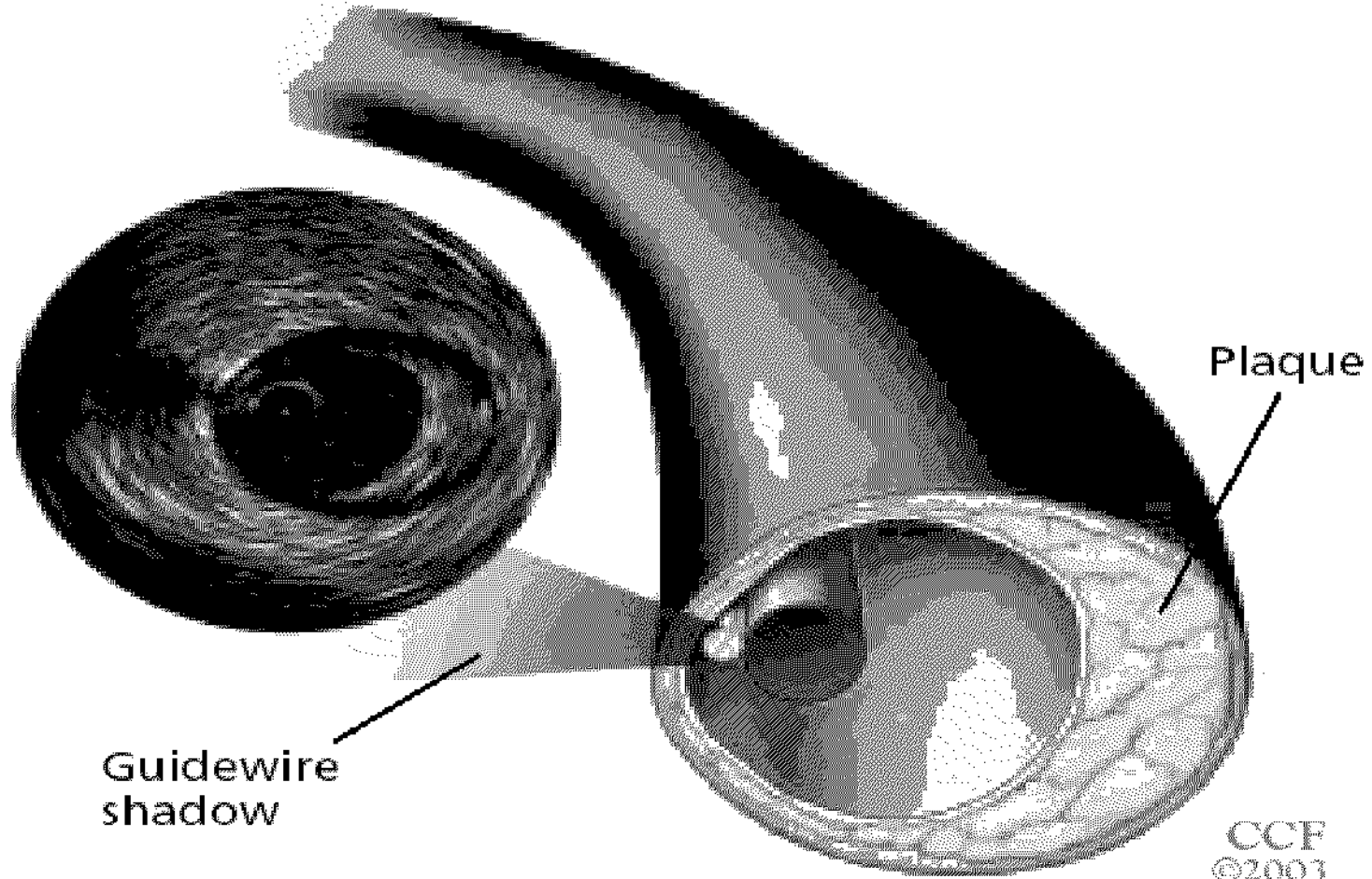
- New diagnostic technology: able to conduct a Phase 2 clinical study
- Identified high quality cardiology group in Canada

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?

Intravascular ultrasonography

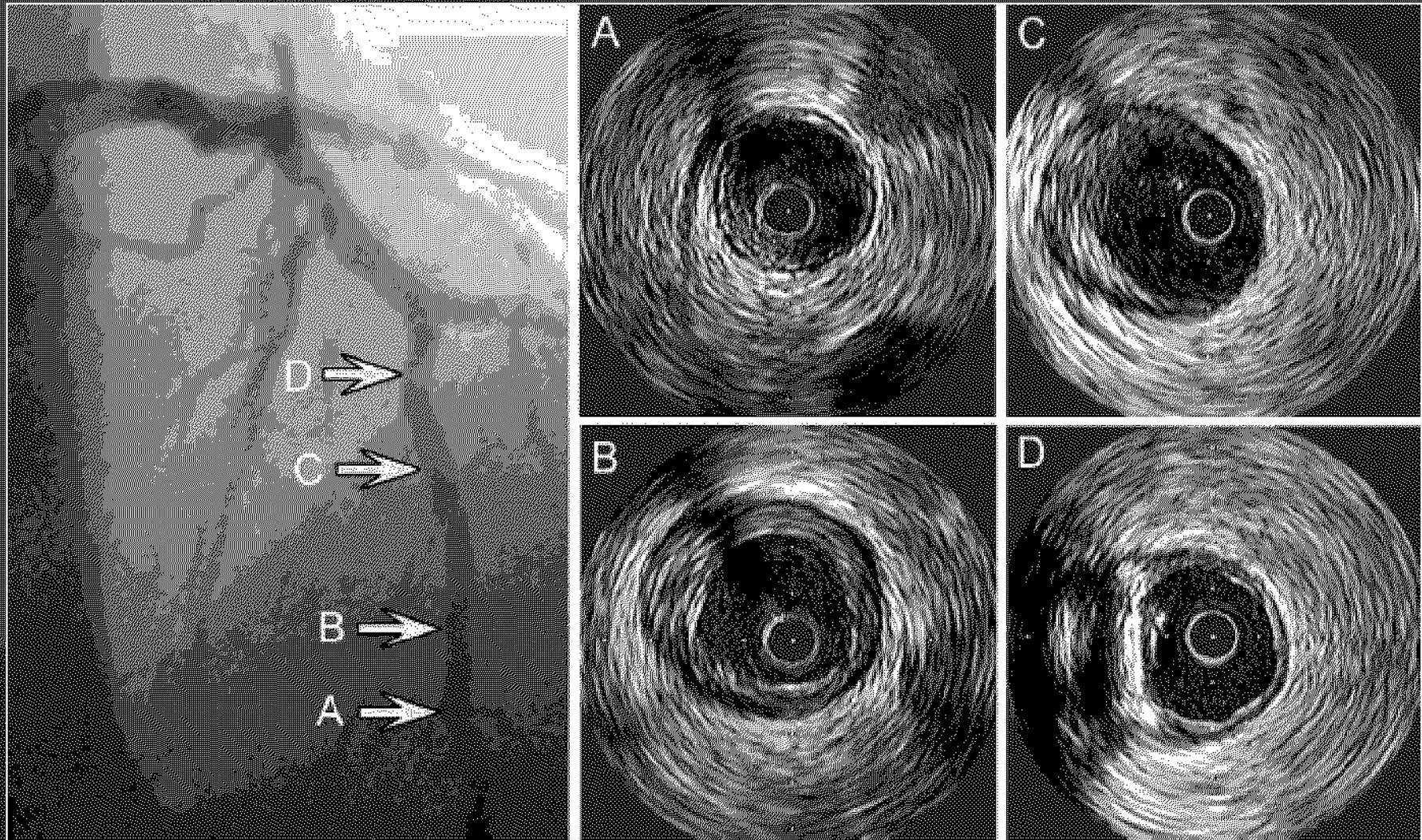


CCF
©2003

Schoenhagen et al, Clev Clin J Med 2003



IVUS shows details otherwise missed



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