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Process versus Product Optimisation

George Lovrecz & Tim Adams, CMSE

AusBiotech Conference, Adelaide 2011



Topics

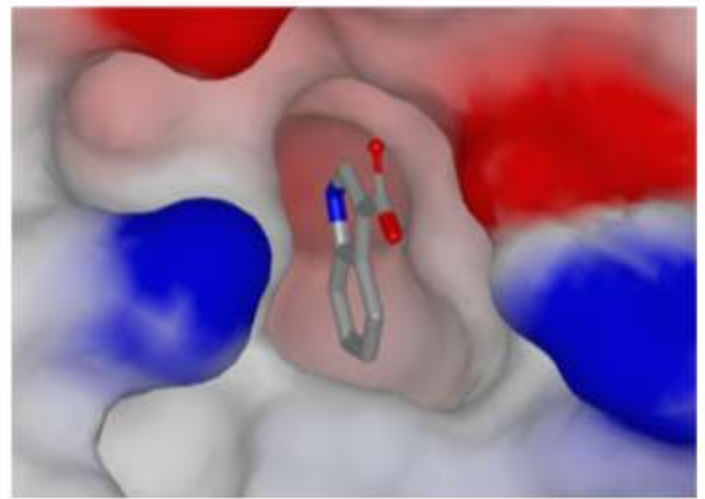
- Introduction of CMSE and the Bioscience Program
- Product design - background - definitions
- What we do at CSIRO



Introduction of CMSE

- Biosciences program ~130 EFT
 - Stem cells, Biomaterials, Structural Biology
 - Biomolecular Engineering
 - **Protein Production/Fermentation**
- Capabilities

Biosciences Program



- **Capabilities**

- C3
- Biological characterisation
- Structural biology
- Fragment based screening



Mini biotech set-up

Gene identification

Gene expression

Scale-up and Fermentation

Protein purification

Crystallisation

X-ray data/3D structure
determination

Molecular modelling

Screen for potential drugs

Biomolecular interaction

Bioassay development

Medicinal chemistry

Animal trials



CSIRO - Australian Biotechnology Growth Partnerships



Process or Product dictates ?

QbD

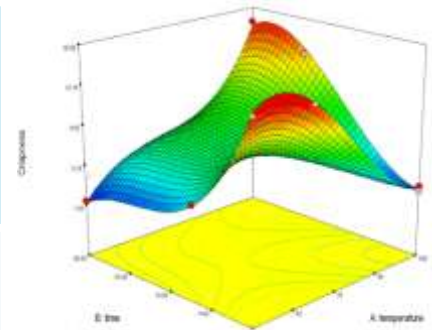
- **Definition**

A systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management.



Quality Control / Assurance

Current QA approach	QbD approach for QA
quality assured by final testing and inspection	quality built in by design based on science
no big picture	knowledge based
specifications based on batch history	based on product performance requirements
rigid system: discouraging changes	flexible within design space, continuous improvement is required
focus on reproducibility, avoiding/ignoring variations	focus on process robustness and understanding & controlling variation

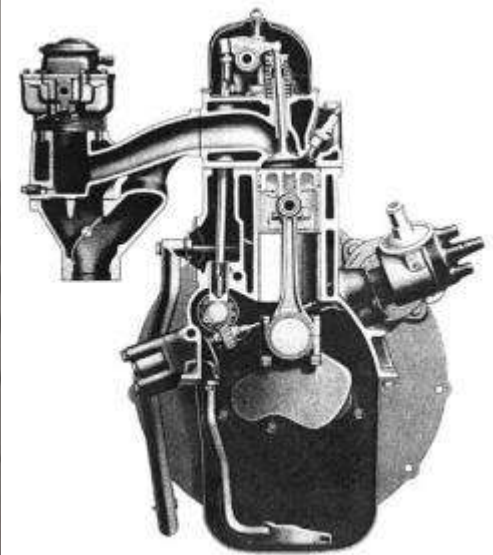


QbD Why this is important ?

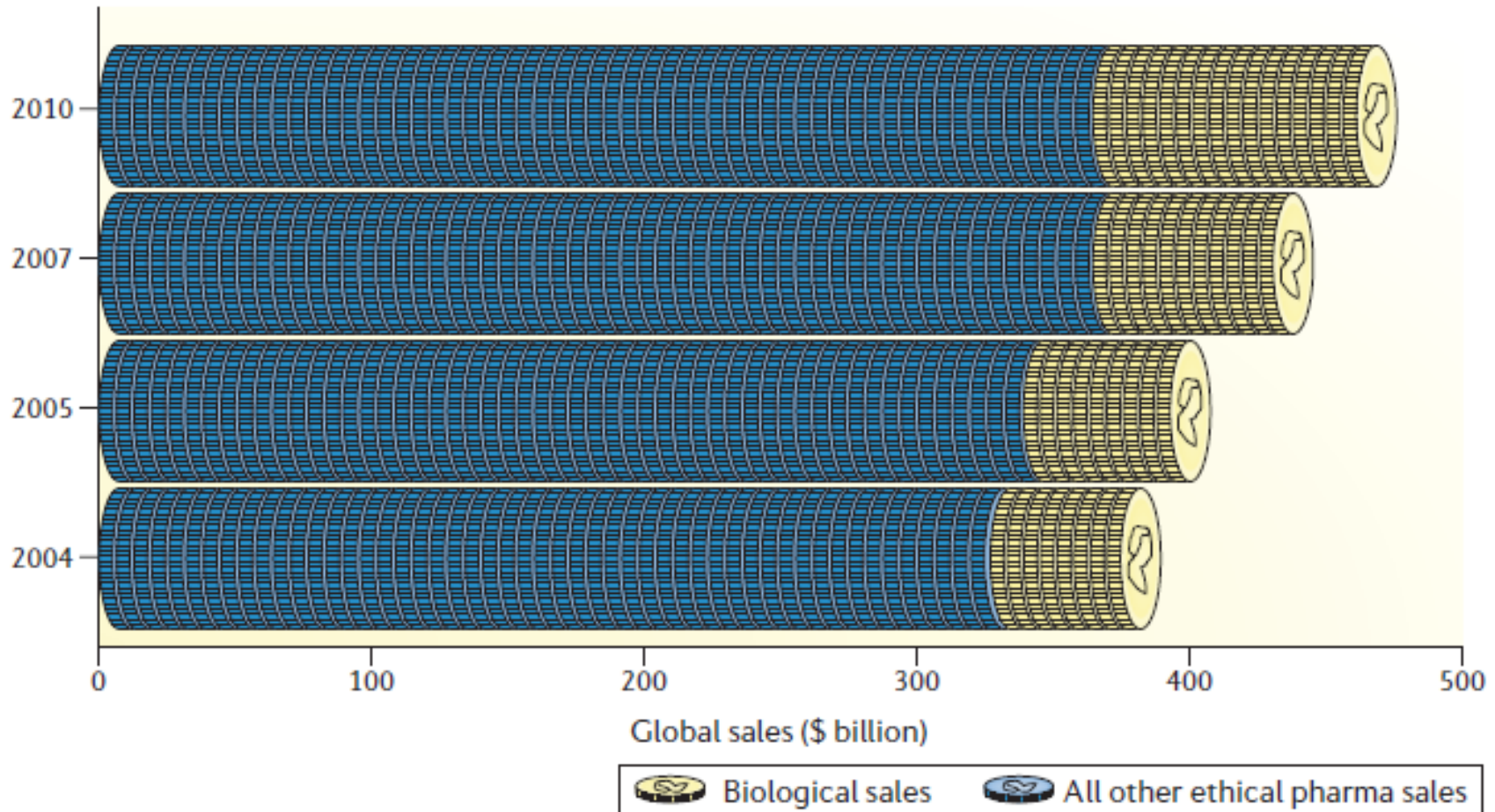
- demand for new technologies



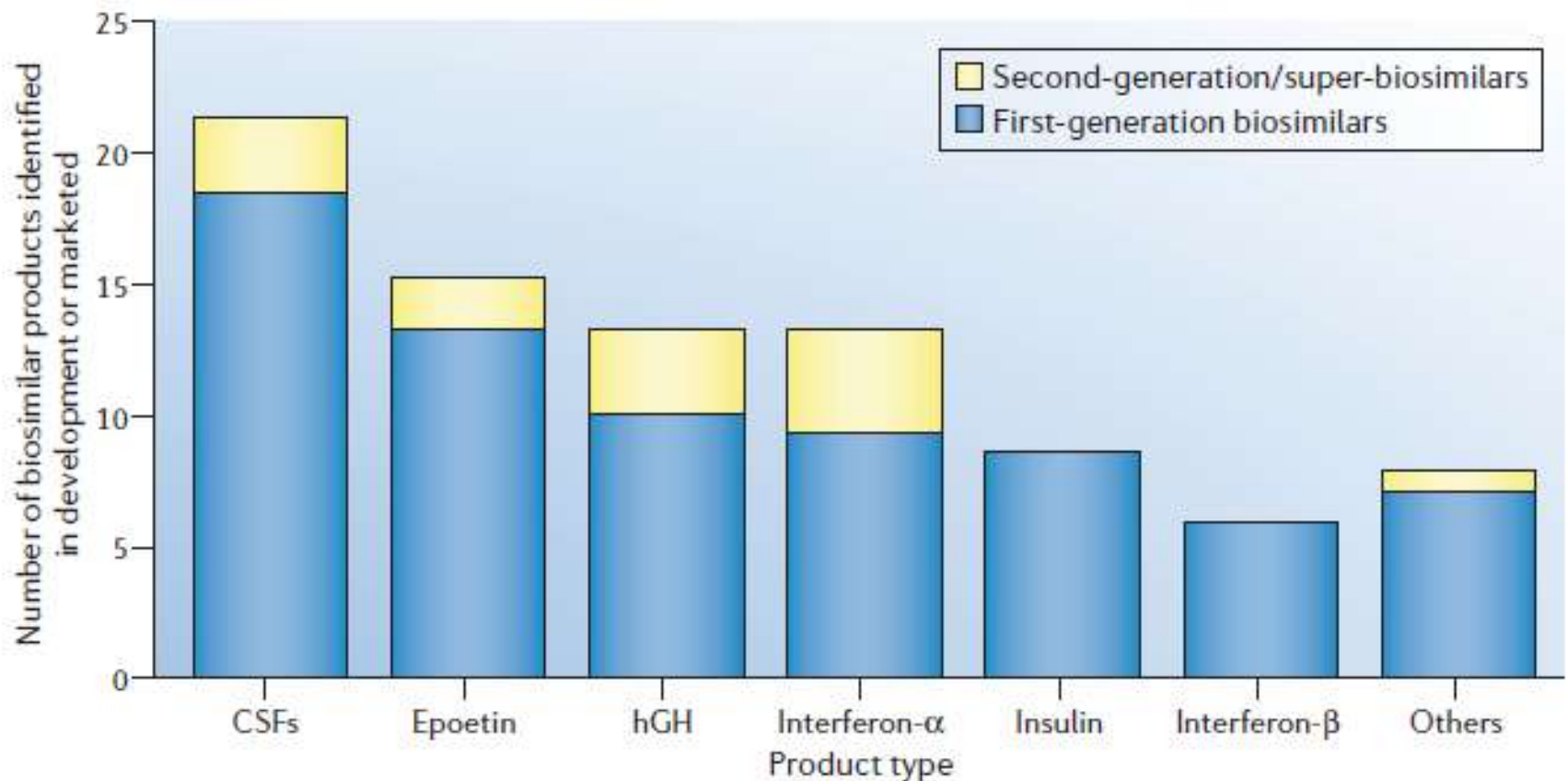
complex



Global sales of pharmaceutical products

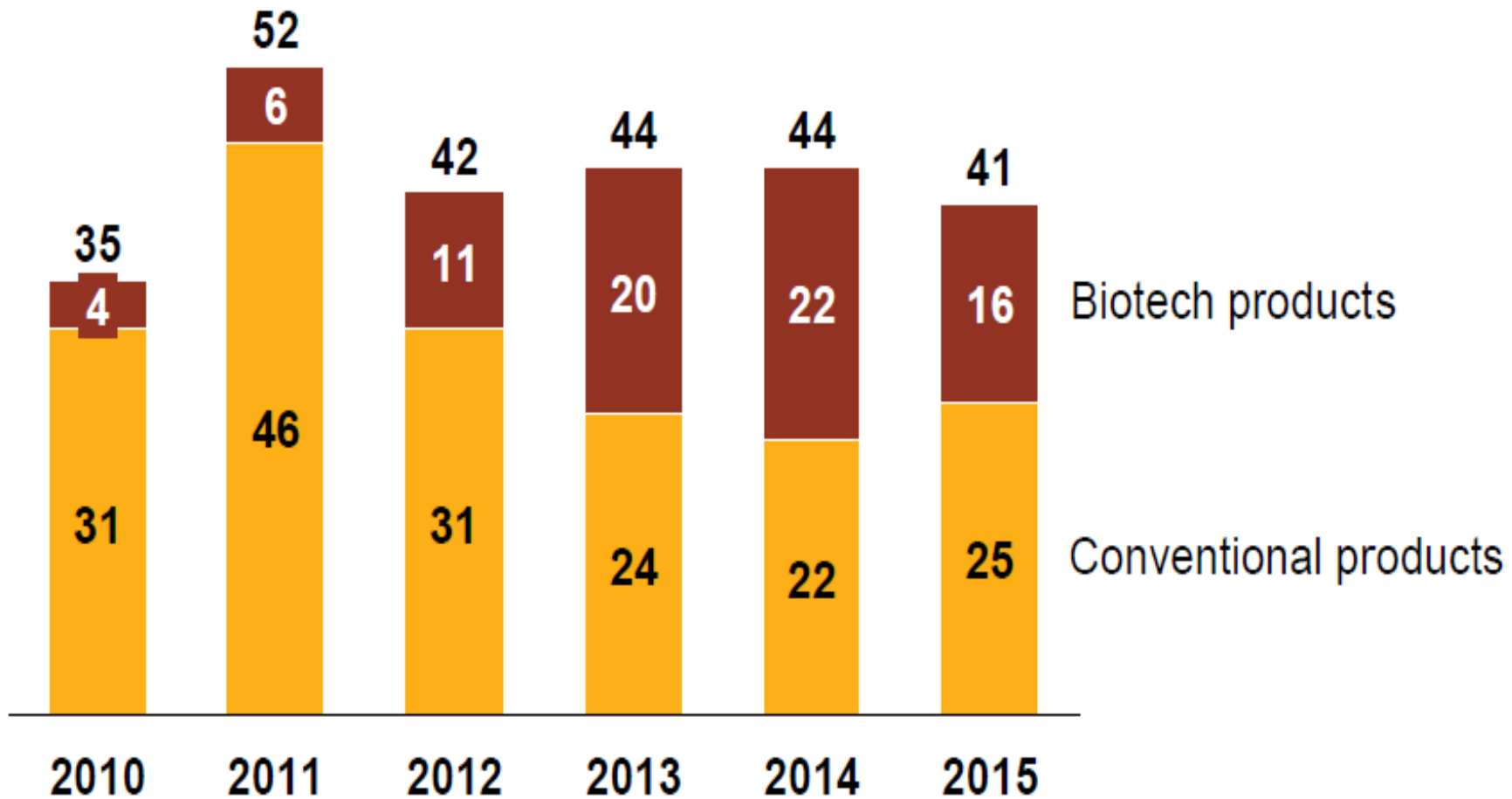


Biosimilars and super-biosimilars



nature/reviews

Patents' expiries drive growth of biosimilars



From: Evaluate Pharma

What we do at CSIRO ?

- **construct and cell line development**
molecular biology, cloning
- **small-scale work / characterisation**
cell banking, transient work
- **scale – up / monitoring**
fermentation modes, vessels, process development
- **purification / biological assays**
formulations, biophysics



Construct and cell line development

- **Focus on product**
- **Mutations, substitutions, deletions**
- **Codon optimisation**
- **Affinity/solubility tags - N- or C-terminal and option to remove them**
- **Host cells – bacterial, fungi, yeast, insect cell, mammalian**
- **Cloning and screening**
Example: HT bacterial cloning and expression in 10 days !



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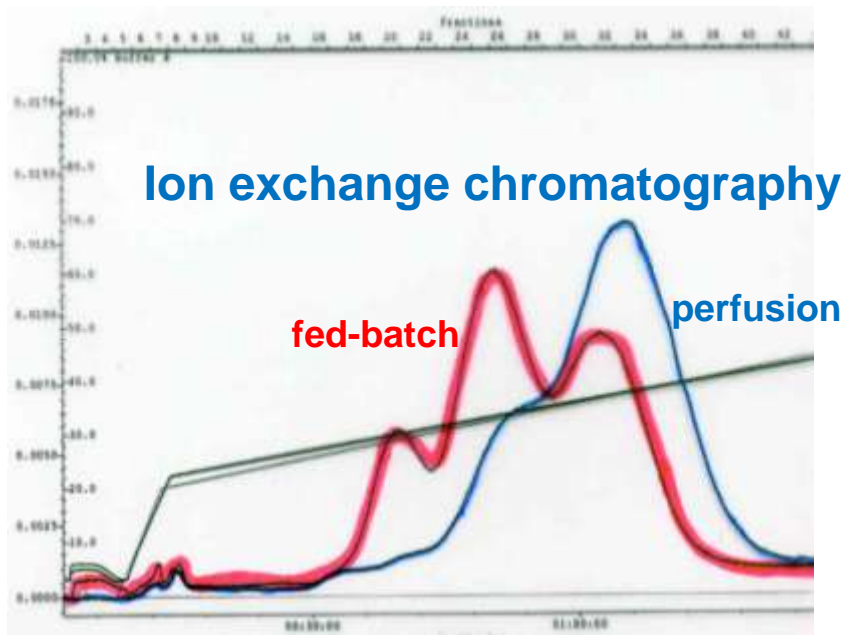
Small-scale work and characterisation

- **Focus on product**
- **Growth and yield determination**
- **Cell banking**
ISO9001 if needed
- **Transient expression to verify quality**
cost effective in-house system for speed !
- **Screening for optimal environmental conditions @ shaker level**
temperature, media/ additives
- **First inputs for harvesting conditions**
essential for insect/baculo virus systems



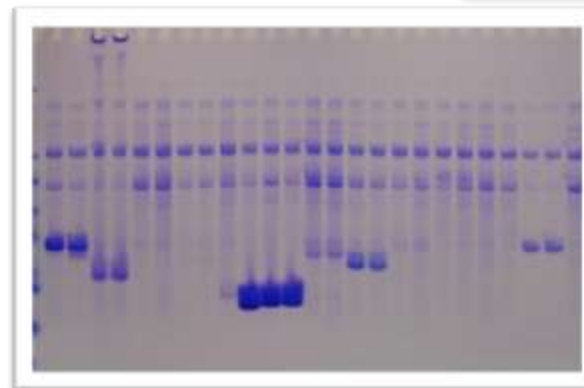
Scale-up and monitoring

- **Focus on product**
- **Vessel / Method / Media**
- **Monitoring**
 - basic parameters on-line
 - metabolic rates at-line



Protein purification and analysis

- Chromatography workstations
- Comprehensive collection of chromatography columns
- Mass spectrometry
- N-terminal amino acid sequencing
- Peptide mapping
- ***Glycoprofiling***
- Biological characterisation (SPR)



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Summary

- **QbD** is here for industry and academia
- It is good for you: adopt asap !
- **CSIRO is a platform technology provider**
 - in-house expertise (cell biology, screening, chemistry, biomaterials and stem cells)
 - small biotech companies and CRCs in Australia

CSIRO Materials Science and Engineering

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Thank you

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