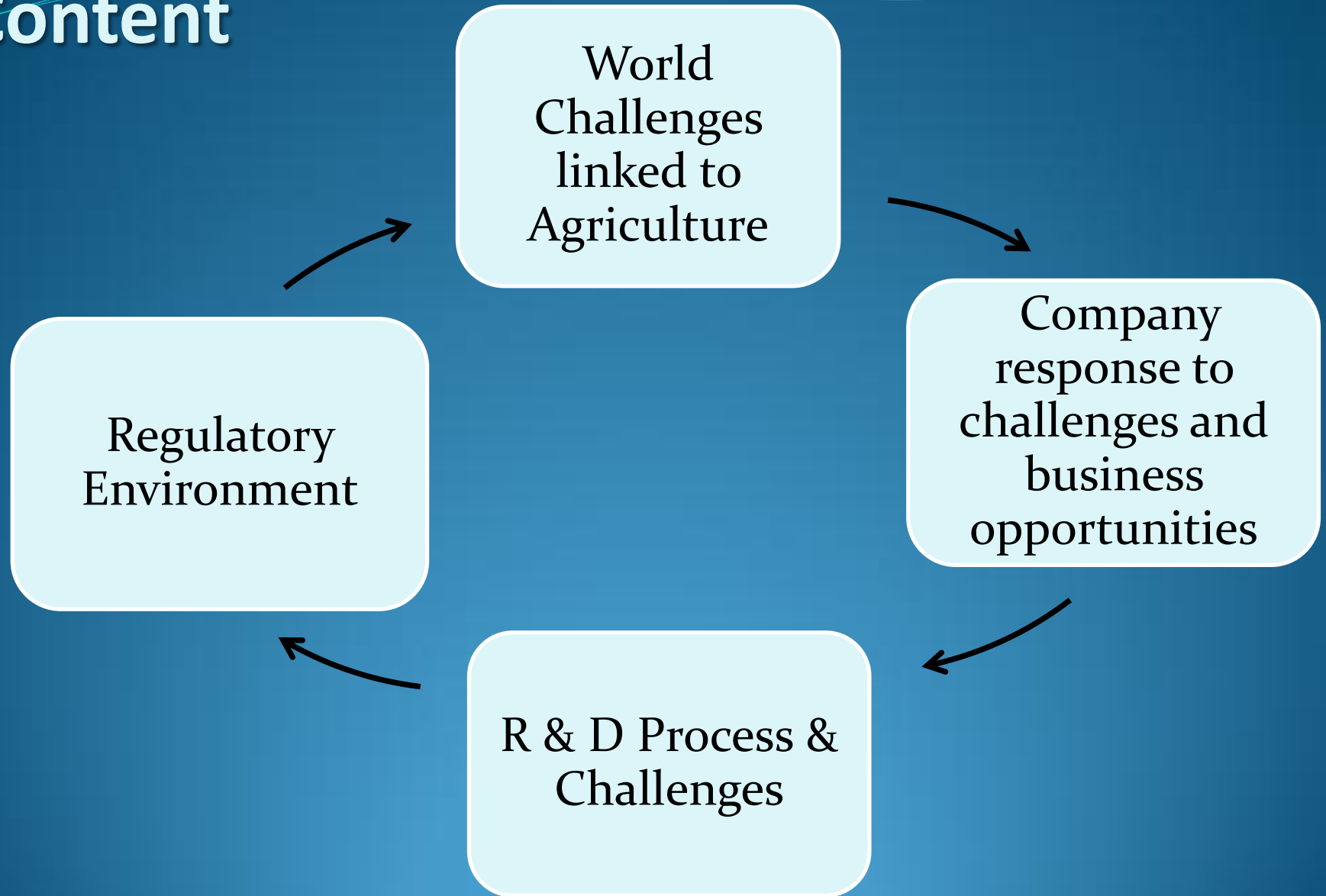


Impact of Regulatory requirements on the development of Plant Protection Products today and in the future.

Richard Maycock

Aug 30, 2011

Content



**World Challenges
linked to
Agriculture**

Critical World Issues

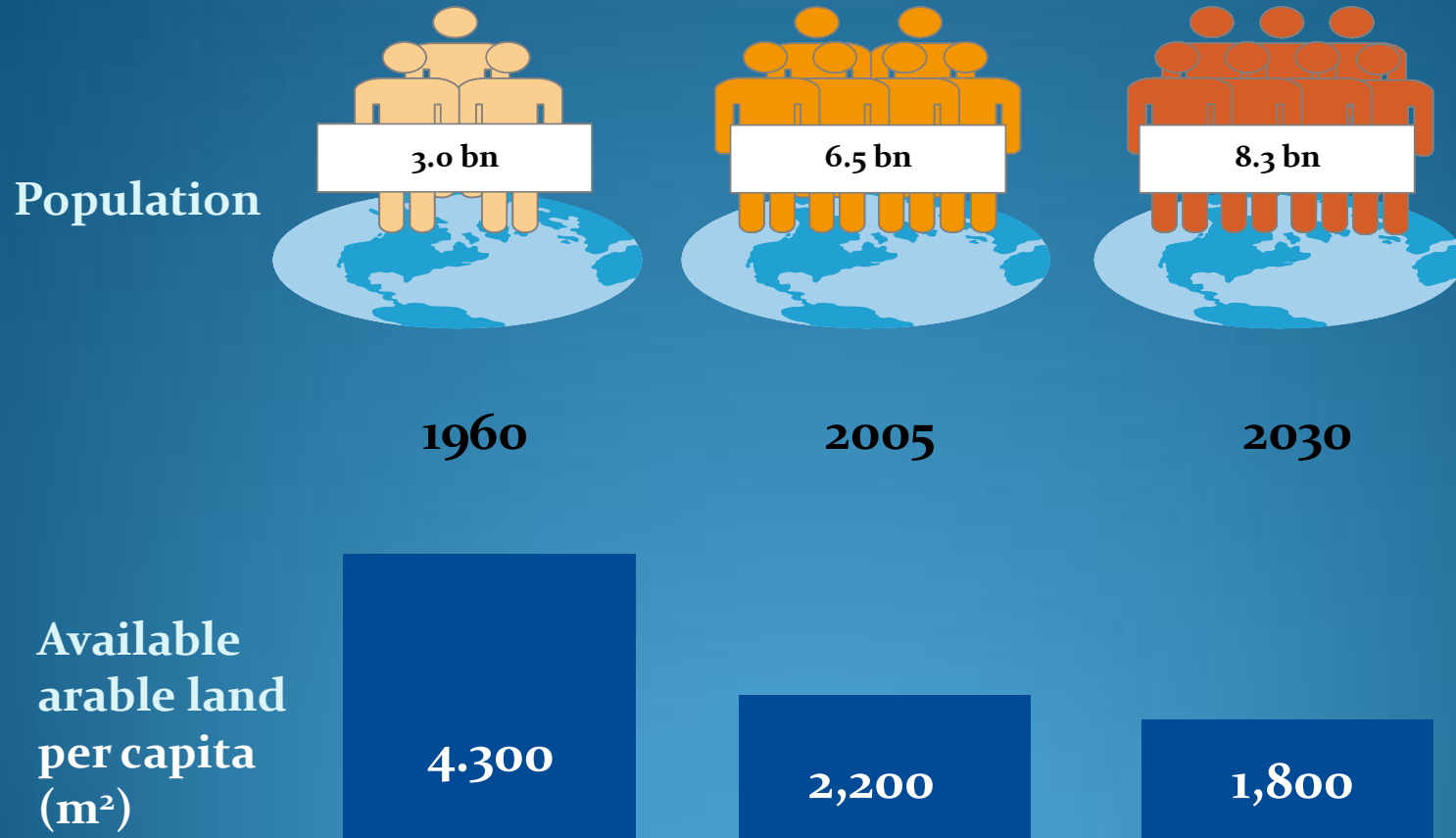
- Energy Security
- Water Security
- Food Security
- Climate Change

Agriculture

Problem ?

Solution ?

We need to Produce More from Less Land

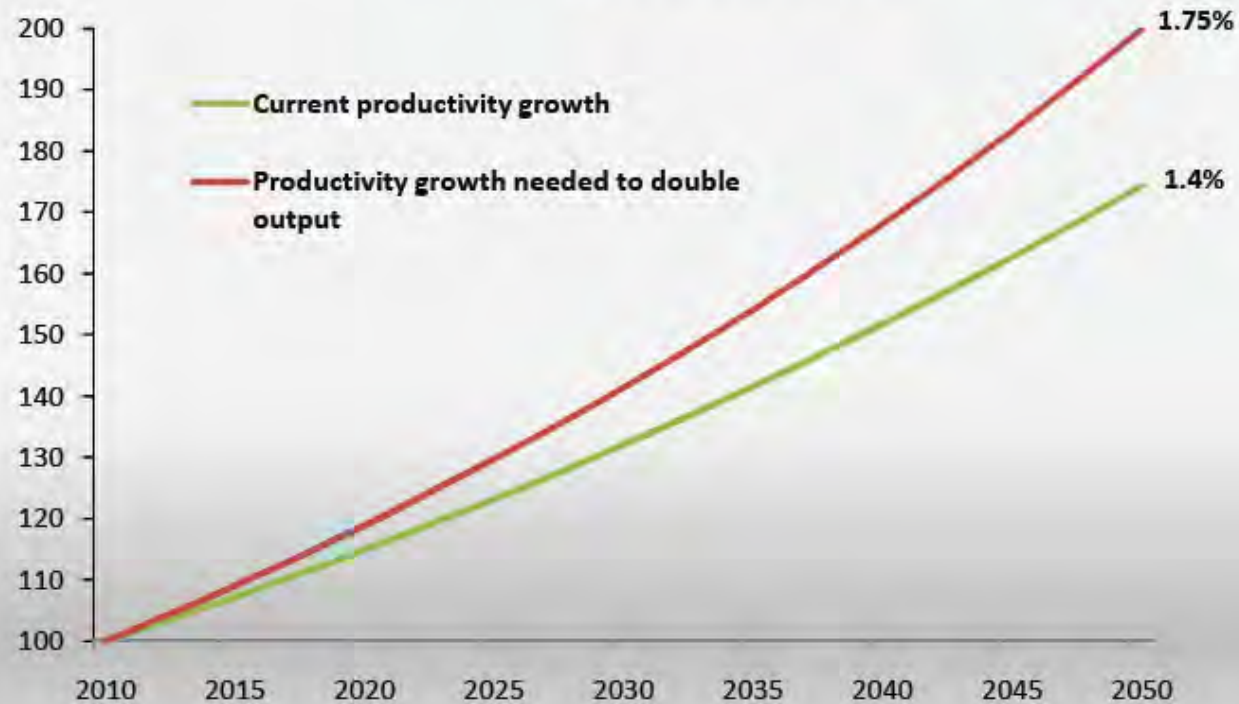


Source: UN, FAO

A Growing GAP

Global Agricultural Productivity GAP

Agricultural Output 2010=100

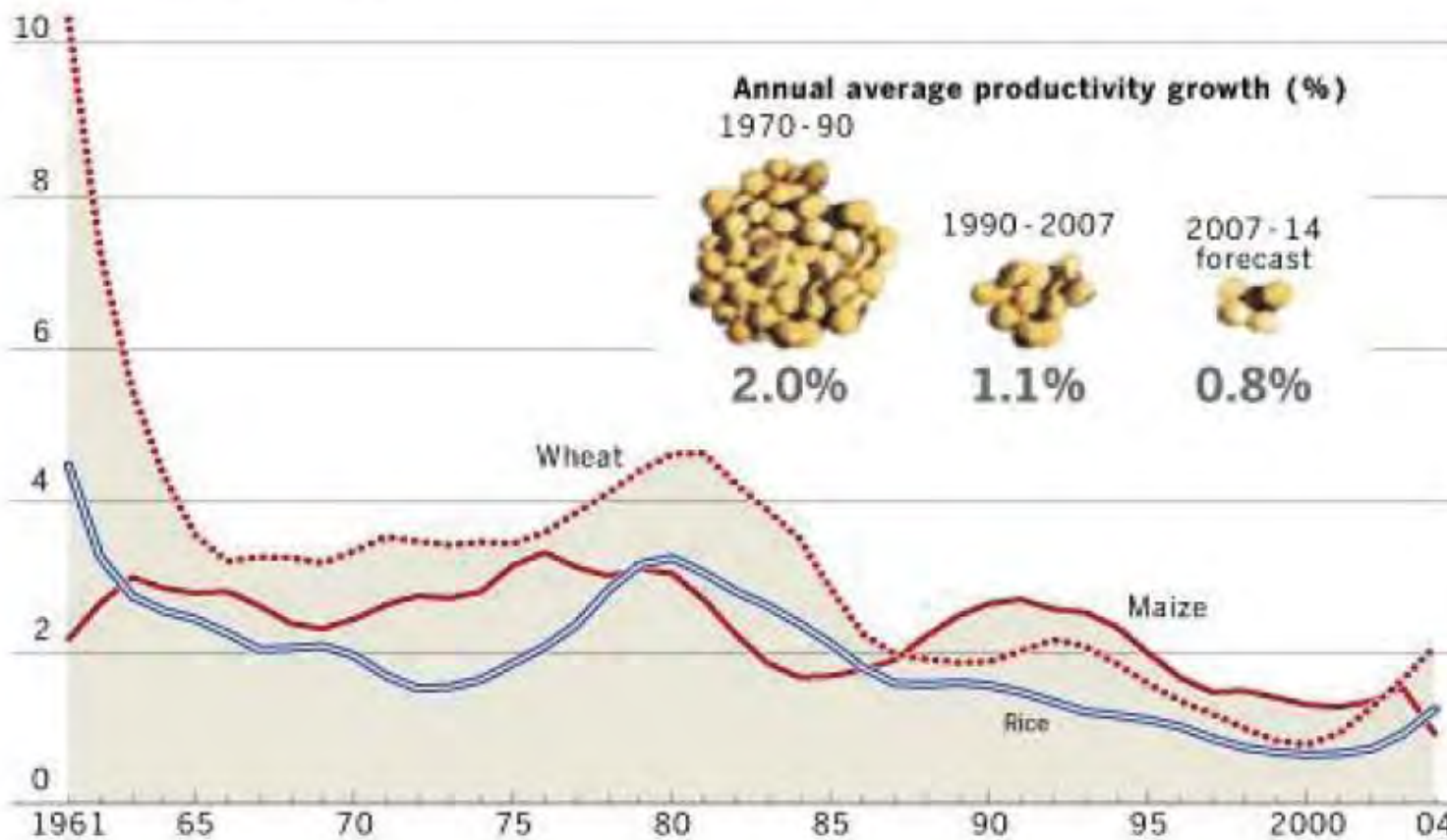


Source: Conklin, Farm Foundation, 2010 GAP Report

Is agricultural productivity growth slowing down?

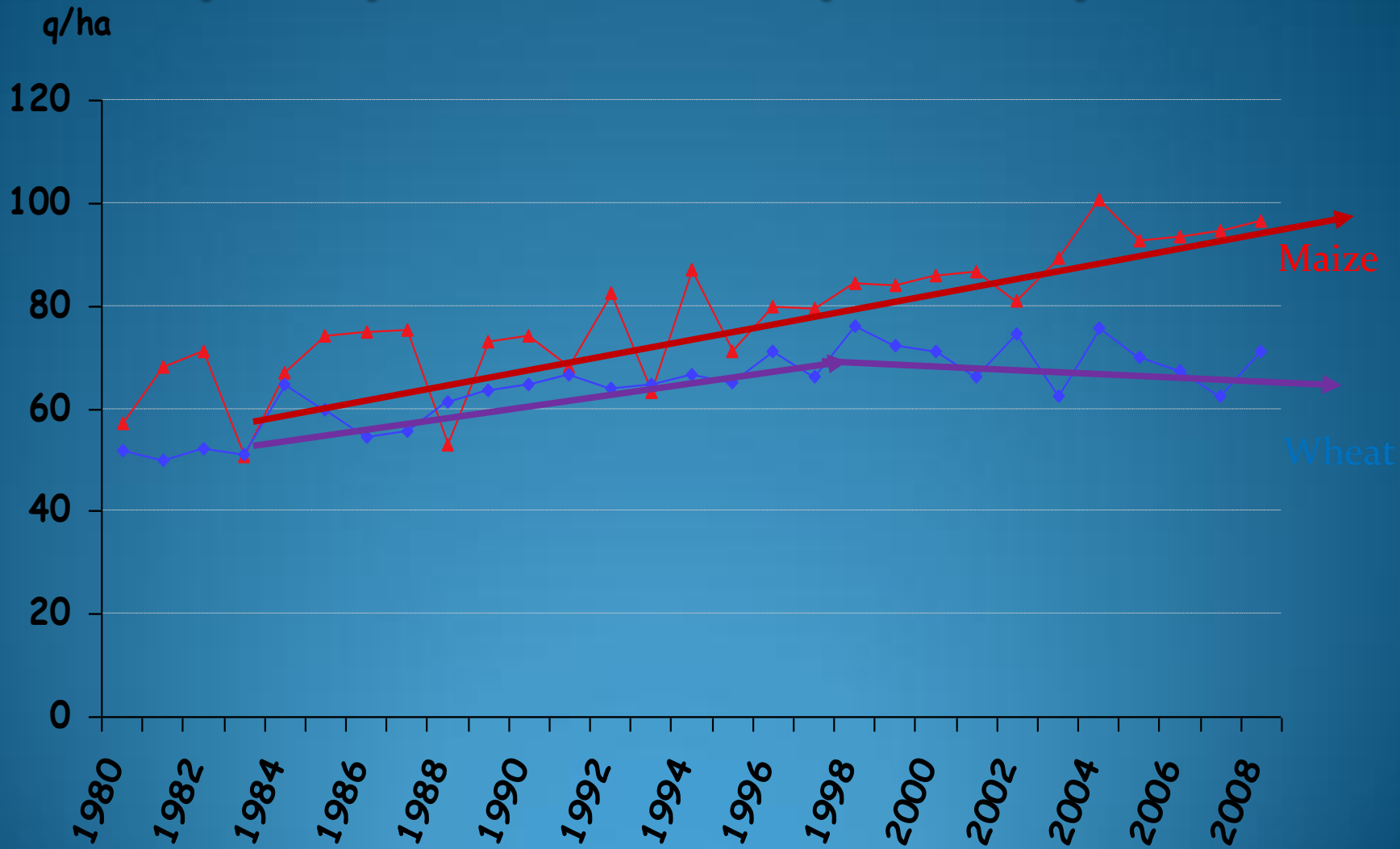
The pace of improvement has slowed steadily...

Annual % change in crop yield



Source: World Development Report 2008, World Bank

Comparison of evolution of yields in maize (USA) and wheat (France)



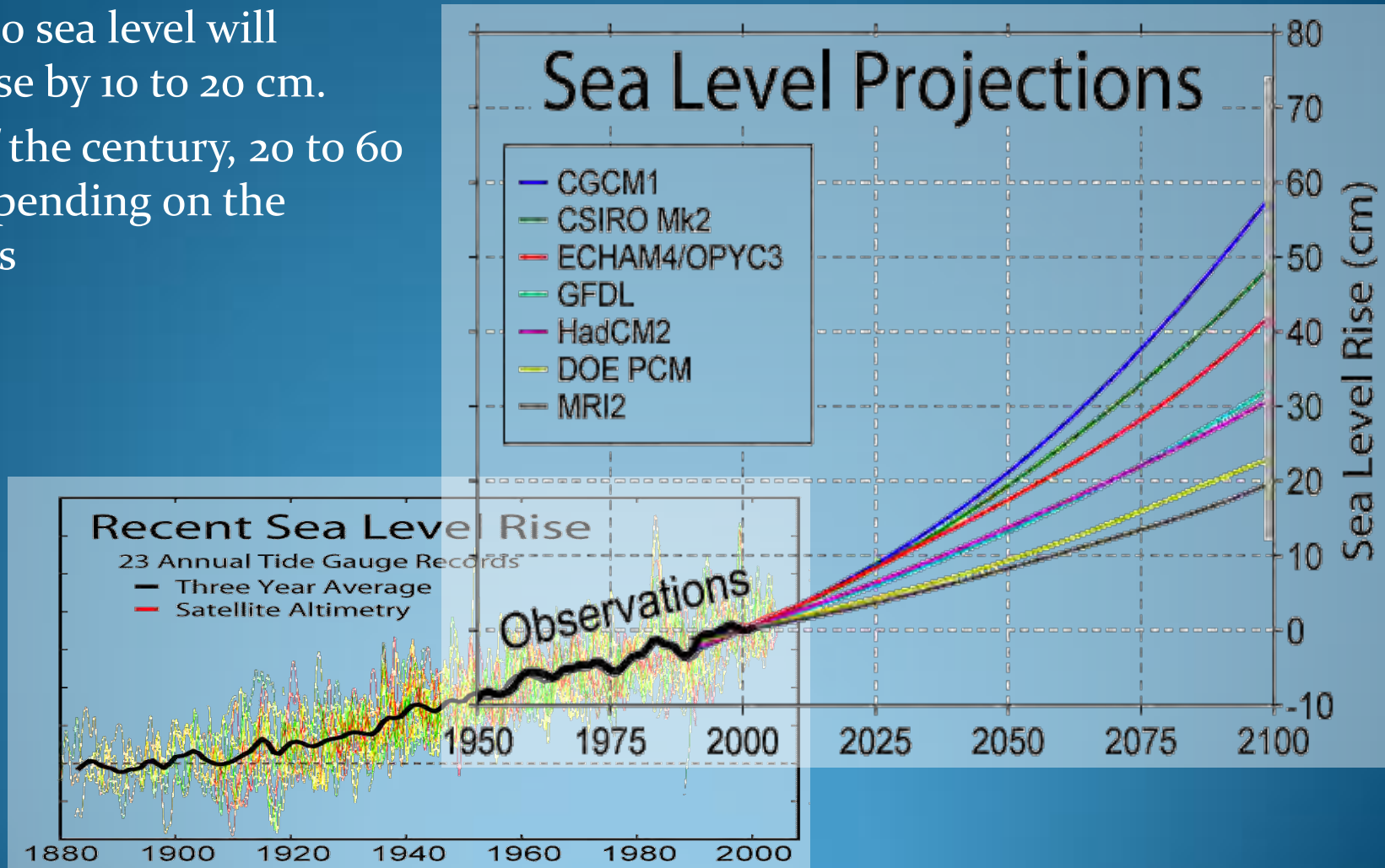
A quotation made by Kofi Annan, at the UN's Food & Agriculture Organization in 2011

“The increasing gap between population and food production growth may turn this years food crisis into a permanent disaster”

“ Delivering global food and nutrition security is the challenge of our time”

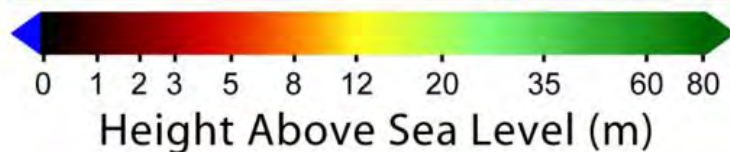
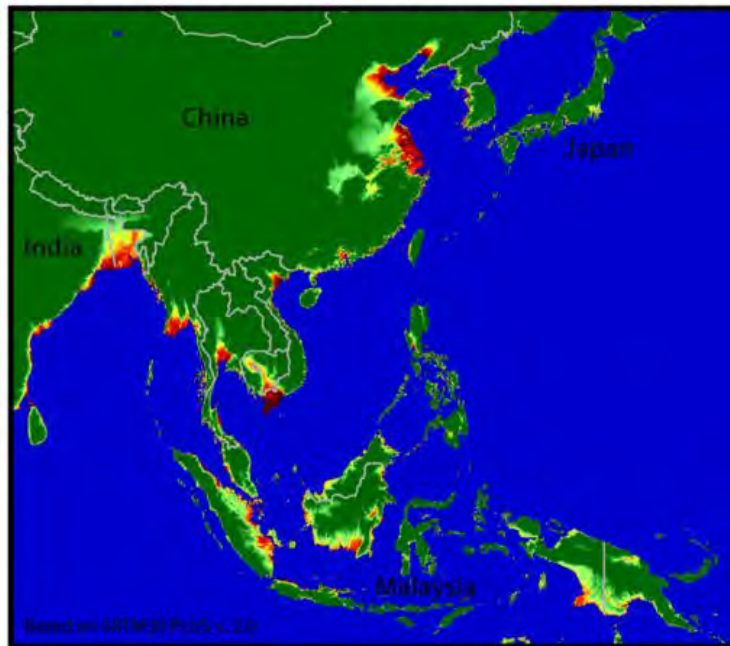
Scenario: Sea Level Projection

- By 2050 sea level will increase by 10 to 20 cm.
- end of the century, 20 to 60 cm depending on the models

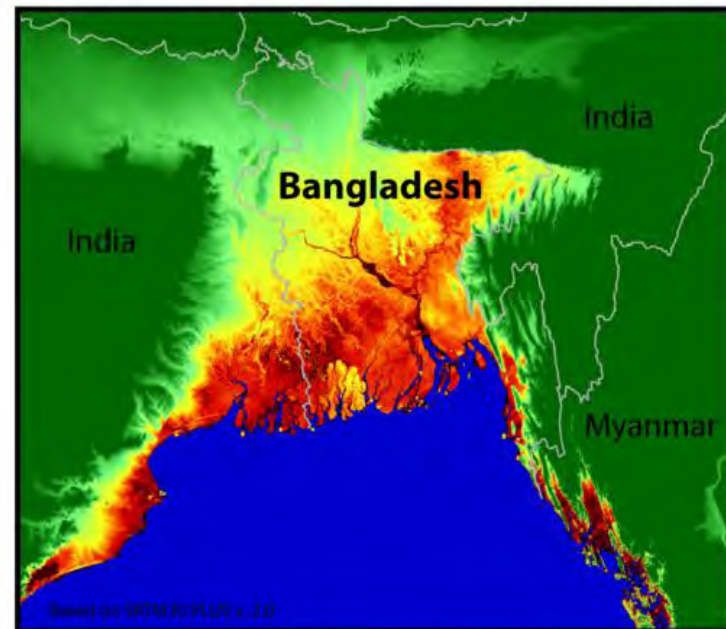


Global Warming Effects: Land at risk in Asia

Sea Level Risks - Southeast Asia



Sea Level Risks - Bangladesh



**Company
response to
challenges and
business
opportunities**

Company Considerations on return on Investments

Political arena in agricultural sector & future landscape

Prediction of future crop commodity & agronomic trends

Current & future market space, & opportunities vs portfolio

IP Position/competitors

Discovery Targets

R&D & Manufacturing Investment

REGULATORY ENVIRONMENT



\$ ROI

Where does the money go ?

- Sales → Taxman



- EBIT/EBITA → Shareholder



- Economic Profit & Borrowing

↘
Reinvestment
(R&D)

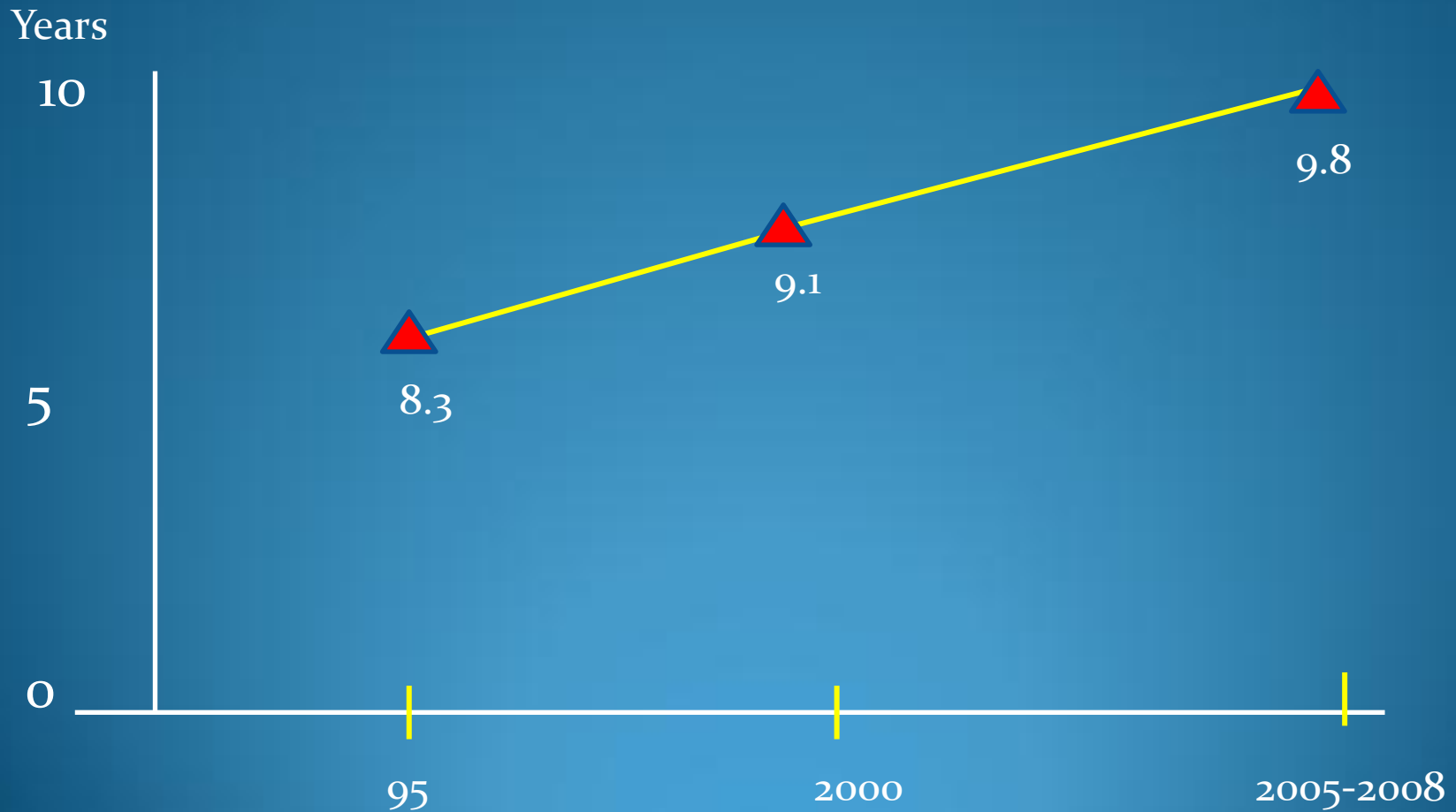


R & D Process & Challenges

Ag R&D Realities

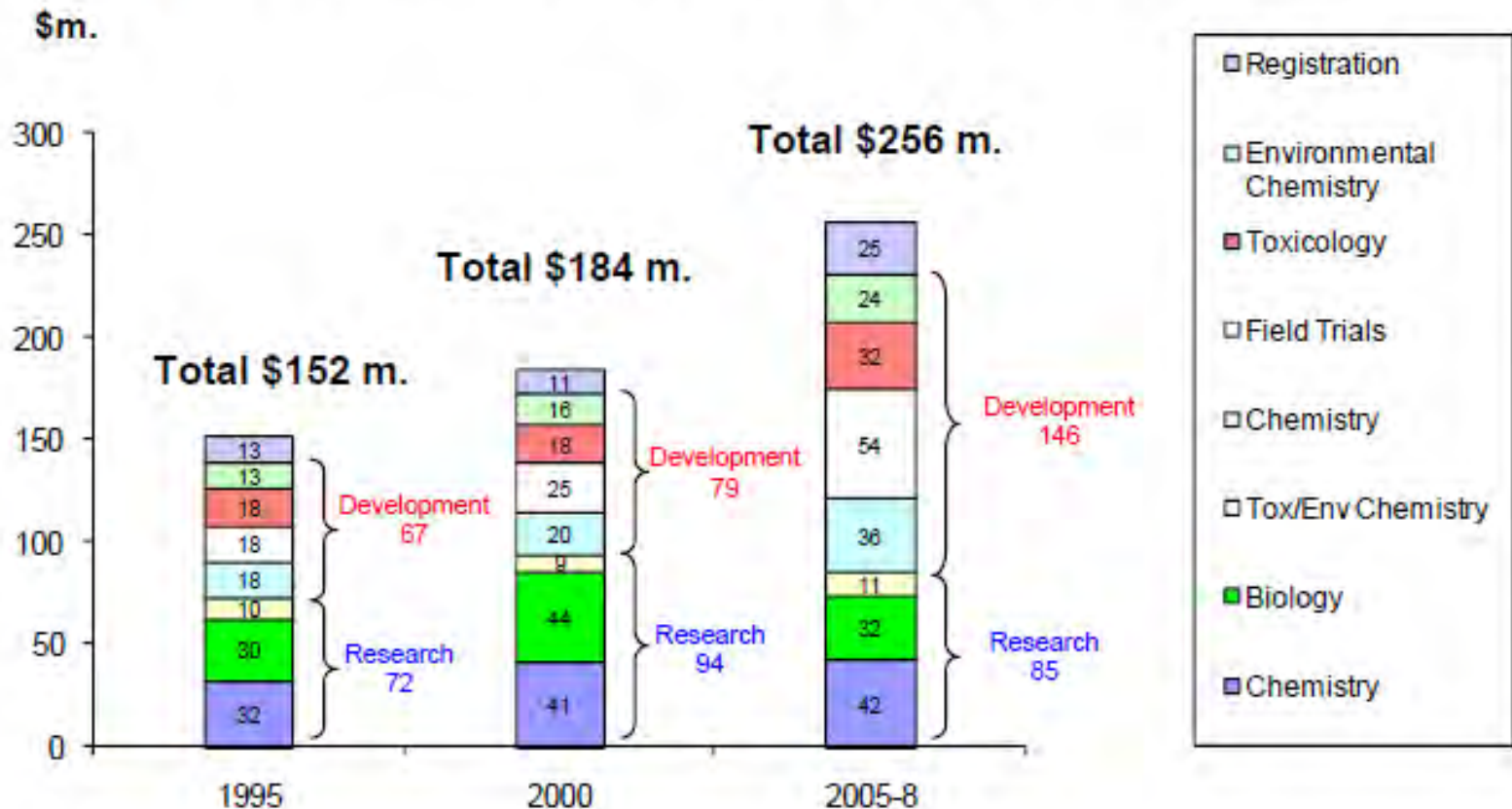
- Nearly 10 years between initial synthesis and initial sales
- Approximately 140,000 candidate molecules screened per one active substance reaching the market
- Cost of R&D for delivering a new active substance has risen by approximately 50% in the last 10 years
- Increased regulatory requirements have been a major part of this increased cost
- New and increased regulatory requirements have started to impact the flow of new substances through the R&D process

Number of years between synthesis and first sale

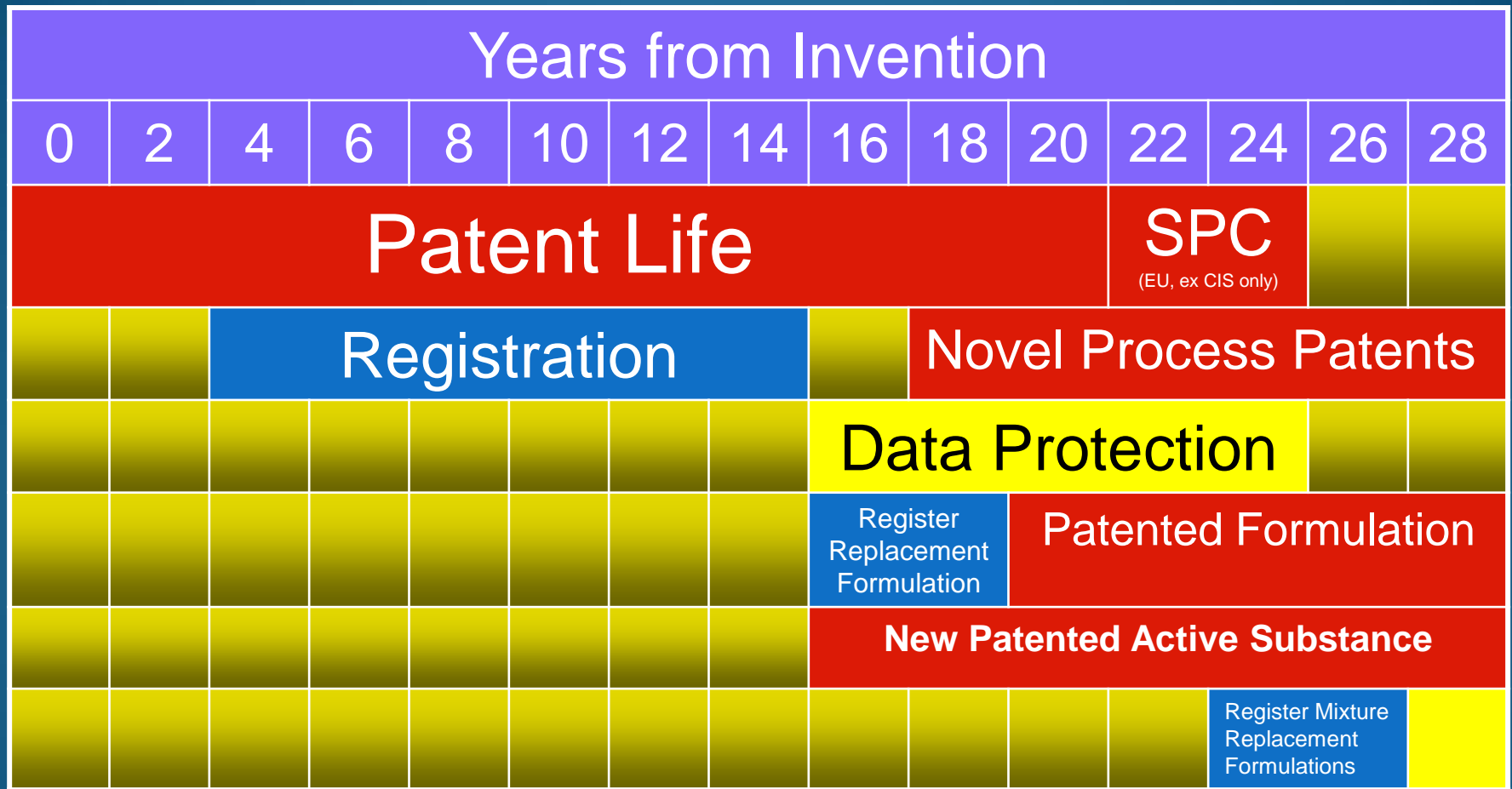


R&D Costs

Discovery and Development Costs of a New Crop Protection Product



Product Life Cycle



Regulatory Environment

Regulatory Environment (EU)

- European Crop Protection Primary Legislation
 - Directive 91/414
 - **NEW** Regulation 1107/2009
- Other European Legislation
 - MRL Regulation 396/2005
 - Water Framework Directive 2000/60
 - Dangerous Substances Directive 67/548
 - Dangerous Preparations Directive 1999/45
 - **NEW** Classification, Labelling and Packaging Regulation 1272/2008
 - **NEW** Sustainable Use Directive 2009/128
 - **NEW** The REACH Regulation 1907/2006

Impact of 91/414

Stage	No actives	In	Out	Pending
1	90	55	35	0
2	148	34	114	0
3	394	114	265	15*
4	326	111	214	1*
Total	958	314	628	16*
New	171	93	8	70
Total Incl. new	1,129	407	636	86

* Awaiting final vote or council decision

Source ECPA, Aug 2011


Impact on loss of active substance from the market

- Loss of actives has removed valuable chemistry from the farmers 'toolbox'. This includes less options for IPM.
- Loss of actives reduces potential income and re-investment in new innovative technology
- Loss of actives combined with higher regulatory hurdles has reduced the flow of new active substances through the development process.
- Resistance Action Committees have been clear in the need to maintain the 'toolbox' for different modes of action in order to combat growing resistance threat e.g. no new herbicide with new mode of action for over 20 years


1107/2009 Hazard Criteria/Candidates for Substitution

- Persistent, Bioaccumulative and Toxic (PBT) (Annex II 3.7.2)


Persistence					AND Bioacc.	AND Toxicity			
Water (DT ₅₀ , d)		Soil (DT ₅₀ , d)	Sediment (DT ₅₀ , d)		BCF in fish	Aquatics	Mammalian		
Fresh or estuarine	OR Marine	OR Soil	OR Fresh or estuarine	OR Marine		NOEC marine or fw	CMR	CMR	STOT
>40	>60	>120	>120	>180	>2000	<0.01 mg/kg	Cat 1a or 1b	R Cat 2	RE 1 or 2




HB




FU



HB



IN



FU

- 2/3 PBT ⇒ Candidate for Substitution
- Commission to draw up list from approved actives by Dec 2013

Estimated losses from environmental hazard criteria under 1107/2009

Group	Cut off		Candidates for substitution	
	Total	POP/PBT/ vPvB	Total*	2/3 PBT
Insecticides	6	3	22	11
Fungicides	25	1	15	10
Herbicides	11	1	26	25
PGR	1	-	1	-
Rodenticide	1	-	1	-

Source: UK PSD assessment Nov 2008 based on published data

Assessment includes some actives which subsequently have not gained approval.

* Does not include actives already triggering the cut-offs.

Influence of Regulatory Evaluations from EU & EPA

- Most follow EPA or EU Leadership in terms of & Guidance & regulatory evaluation output
- DAS survey found 78% of countries internationally were directly or indirectly influenced by these government regulatory assessments

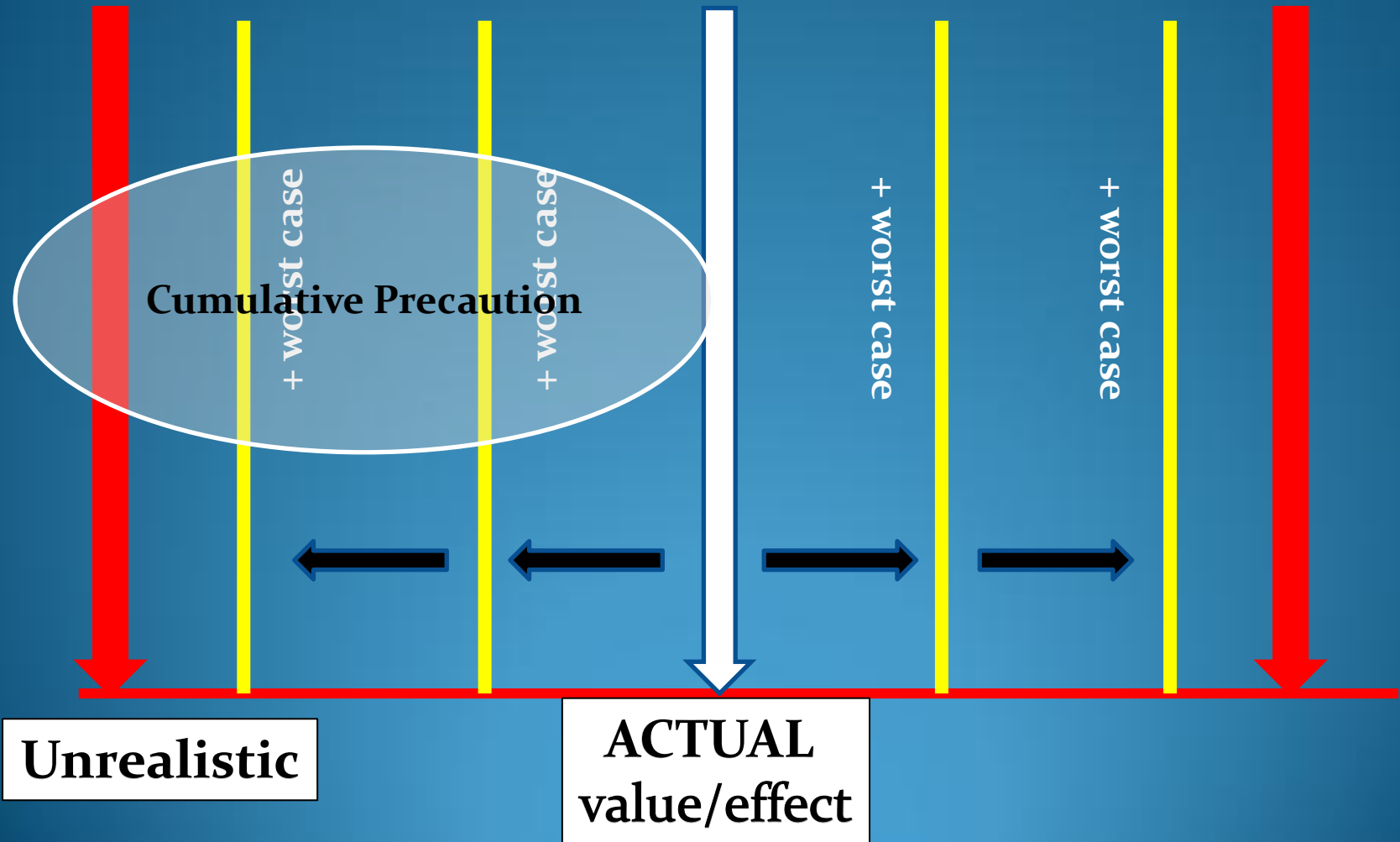
Exposure Assessments - metabolites

- Growing emphasis on metabolite exposure and risk evaluations
- Particularly difficult to evaluate fate and behaviour of tertiary metabolites
- Do we have sufficient accuracy and precision of relevant studies when quantifying tertiary metabolites?
- Has the regulatory need outstripped the ability of the study to provide the relevant quality answers?

Leads to:

- Further extensive & expensive testing
- Further evaluation & resource drain from agencies and company
- Possible more relative time spent on a metabolite than active substance 'skewed'
- Possible loss of substance
- Uncertainty in other agencies

Realism



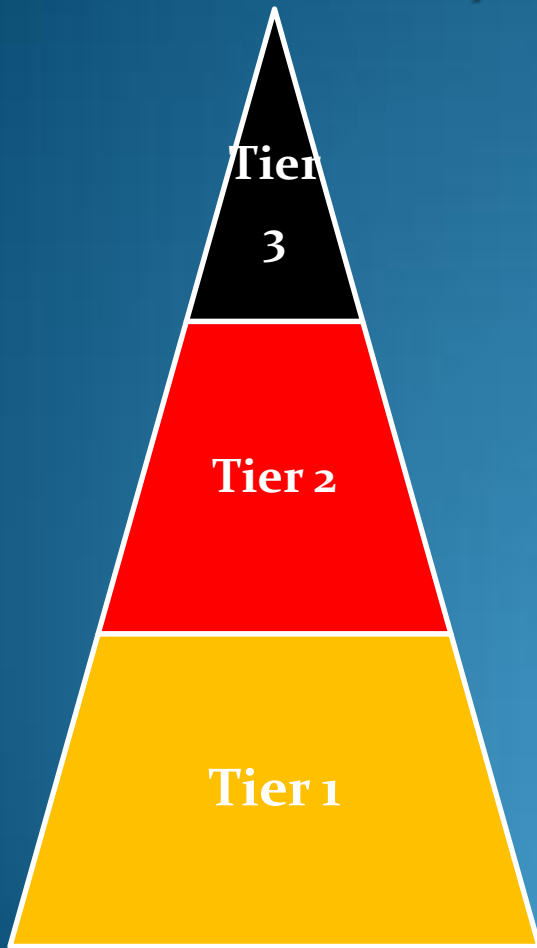
The Simplicity-Complexity dilemma

Data Availability

Complexity

Relevance

Cost



Realism

- Higher Tier data though expensive should be at the centre of evaluations where appropriate
- Will help drive towards 'real' risk or exposure
- EU, EPA, National Agencies, Academia & Industry need to continue to determine the best approaches & study designs for generating higher tier data

Risk Management

- Must learn from the history of the molecule & its use
- Concerted effort to understand the details of how the assessment was conducted & the degree precaution used in the assessment
- Use an integrated approach of determining real risk under use conditions
- Benefits should become an integrated part of the decision making.
- Industry should and will make further improvements in providing confidence in the use of products through more concerted stewardship efforts