Are you ready for the MODA of all portfolio prioritization approaches or is SODA still appropriate?
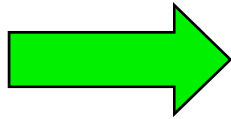
Jeff Stonebraker, Ph.D.

Bayer

**Biological Products
Strategic Planning
Research Triangle Park**

**Prepared for the Decision Analysis Affinity Group Conference
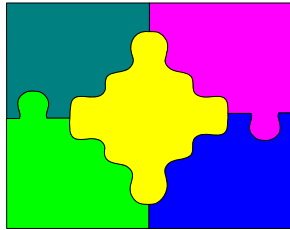Houston, Texas
May 16-18, 2001**

AGENDA

PORTFOLIO PRIORITIZATION: THE CHALLENGE & SOLUTION
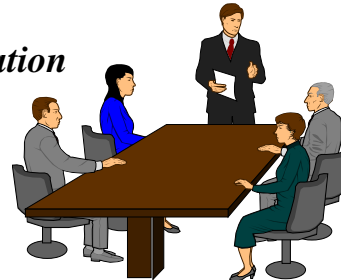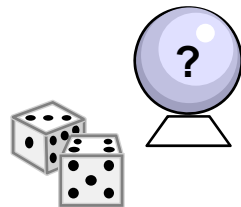
DRUG R&D DECISION-MAKING PROCESS

APPLICATION

The enormous costs and long timelines for R&D as well as the staggering odds against technical and commercial success make portfolio decisions critically important and challenging.

Interdependence among projects

Uncertain & changing technical and commercial information

Dynamic opportunities

DON'T LOOK BACK

Cross-functional communication
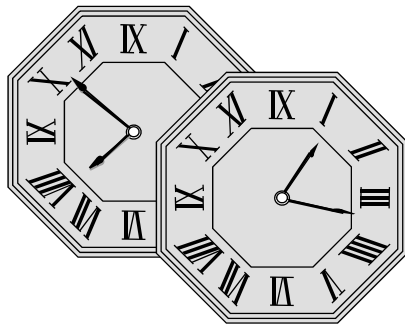
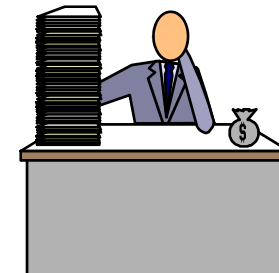**Projects in different stages of R&D**

Decisions

Decisions subject to regulatory & critical review

Investments

Multiple objectives & strategic considerations

Too many projects competing for too few resources

3

What do DECISION-MAKERS want/need to make the best portfolio decisions?

Consistency	Repeatability	Acceptability
Fairness	Effectiveness	Transparency
Defensibility	Efficiency	Completeness
Reliability	Understandability	Comprehensiveness
Timeliness	Clarity	Accuracy
Usable	Believability	Practicality
Relevancy	Quality	Objectivity

We can't do every project.

Some projects are better or more important than others.

We should figure out which projects are better, then do those.

In an effort to ensure that the best portfolio decisions possible are made by decision-makers within the organization, Bayer uses the Dialogue Decision Process ("SDG process").

Steering Committee

| Recognize Situation | Approve Frame | Approve Information | Make Decision | Approve Plan |

Frame   Information   Recommendation   Plan

Core Team

| Create Frame | Collect Information | Evaluate Alternatives | Plan for Implementation |
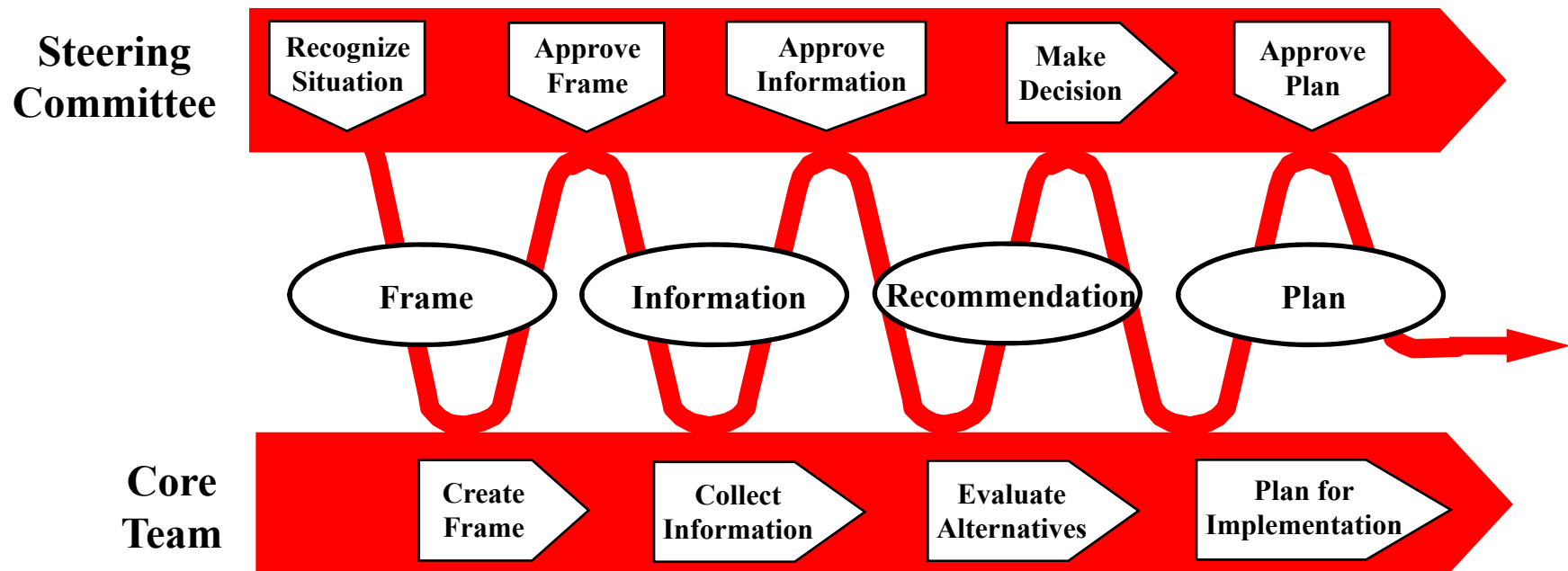
This process was adapted from the Strategic Decisions Group (SDG) and instituted within Strategic Planning at Bayer in the late 1980s.

This process provides a structured interaction between the Steering Committee and the Core Team with key deliverables.

RESPONSIBILITIES

- **Oversee the process and provide a "sounding board"**
- **Approve all critical elements**
- **Manage the process**
- **Create the project evaluation frame**
- **Provide expert judgments and data inputs**
- **Collect information and playback**
- **Construct a decision-focused model**
- **Evaluate the results**
- **Provide data-driven recommendations**
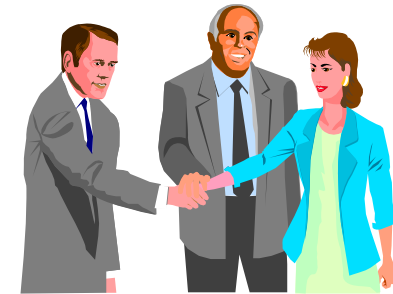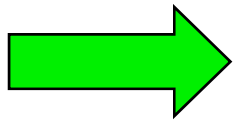

Steering Committee

Core Team

Commitment to action by the organization is possible through due diligence, open review, and fair weighting of evidence.

April 8, 2014

AGENDA

PORTFOLIO PRIORITIZATION: THE CHALLENGE & SOLUTION

DRUG R&D DECISION-MAKING PROCESS

APPLICATION

Bayer has organized its drug R&D into a sequence of decision points (DPs).

DP 0. decision point to begin research

DP 1. decision point to begin pre-clinical development

DP 2. decision point to begin clinical development (Phase I)

DP 3. decision point to continue clinical development (Phase II)

DP 4. decision point to continue clinical development (Phase III)

DP 5. decision point to submit a Biological License Application (BLA)

DP 6. decision point to launch

| Decision Point 0 (DP 0)	→	Decision Point 1 (DP 1)	→	Decision Point 2 (DP 2)	→	Decision Point 3 (DP 3)	→	Decision Point 4 (DP 4)	→	Decision Point 5 (DP 5)	→	Decision Point 6 (DP 6)
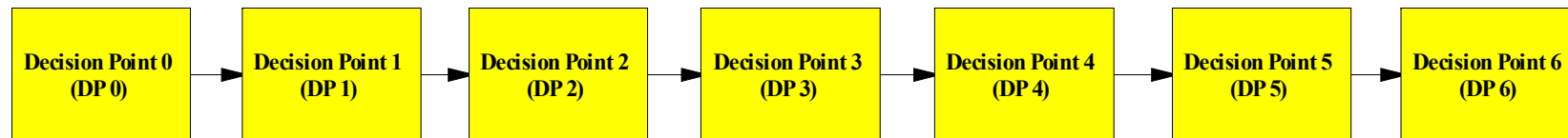
Each project in the portfolio will reside at a certain DP with various scientific and market-related deliverables, include a project decision analysis

The outcome of each decision point is uncertain (technical feasibility).

|	Notional transition success rate	Probability to reach market
Research (DP 0)	10%	1%
Pre-clinical development (DP 1)	50%	10%
Phase I clinical development (DP 2)	75%	20%
Phase II clinical development (DP 3)	40%	27%
Phase III clinical development (DP 4)	75%	68%
Registration (DP 5)	90%	90%
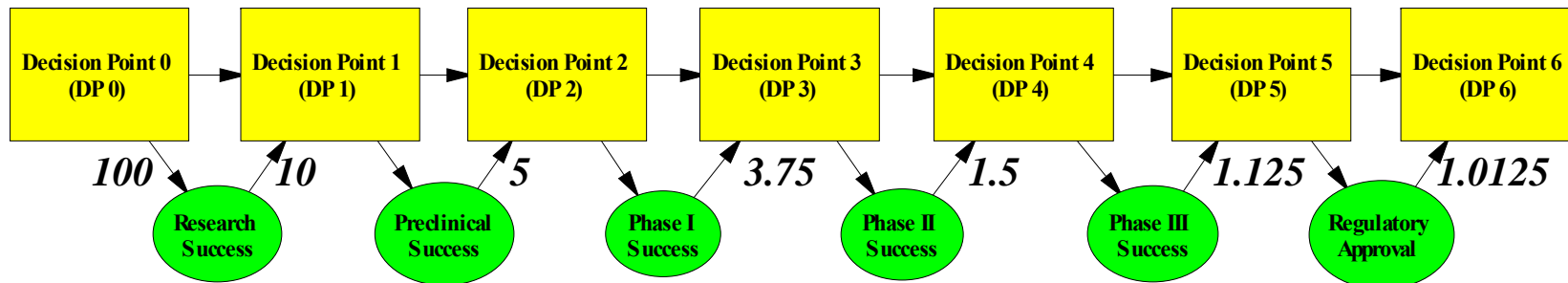
There are also costs (and timelines) associated with each decision point.
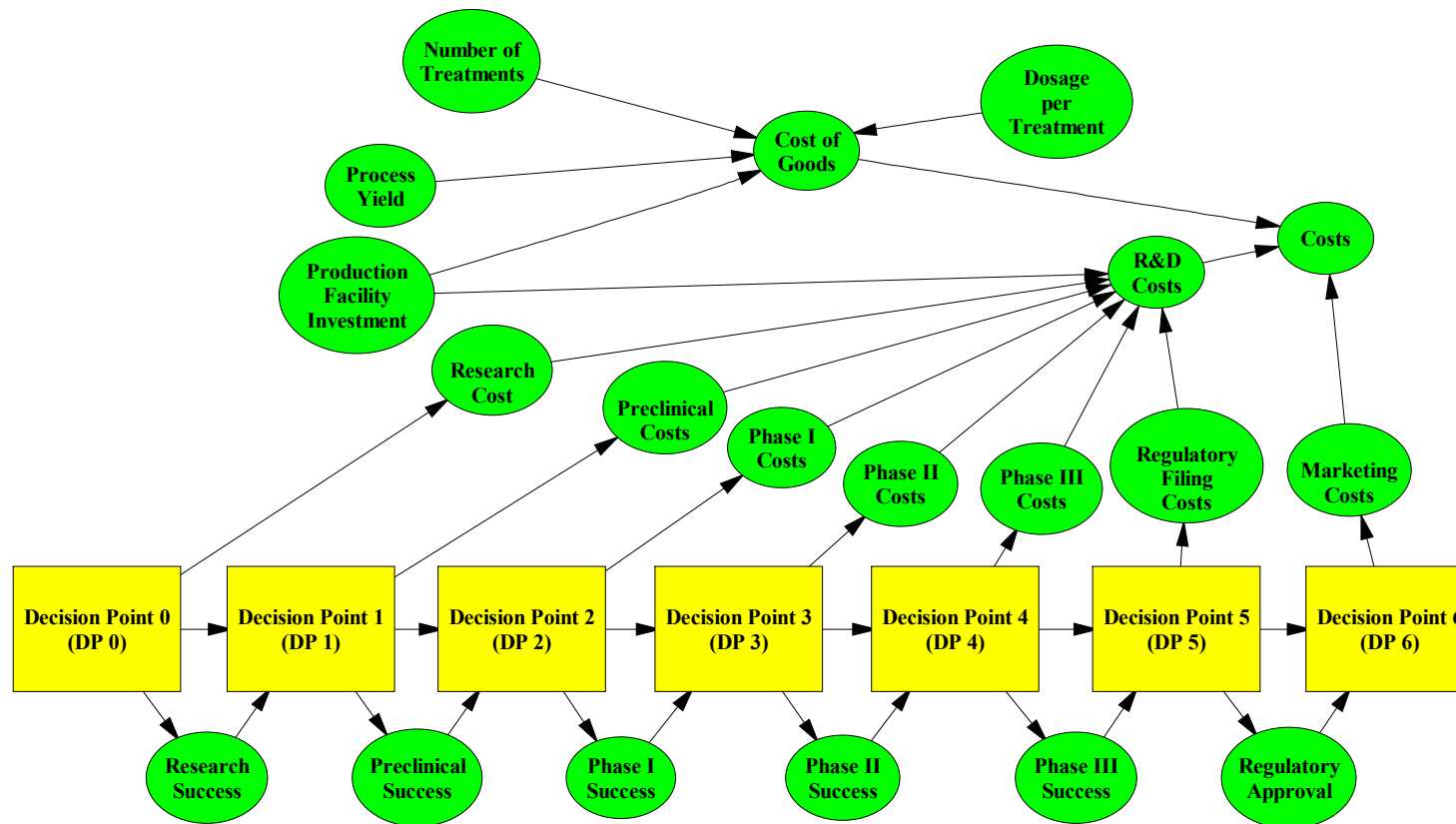
Even if drug development is successful, there are no guarantees of commercial success once the new product is launched into the competitive marketplace.

Notional New Product Life Cycle

Research | **Development** | **Sales ramp up** | **Peak sales** | **Decline**
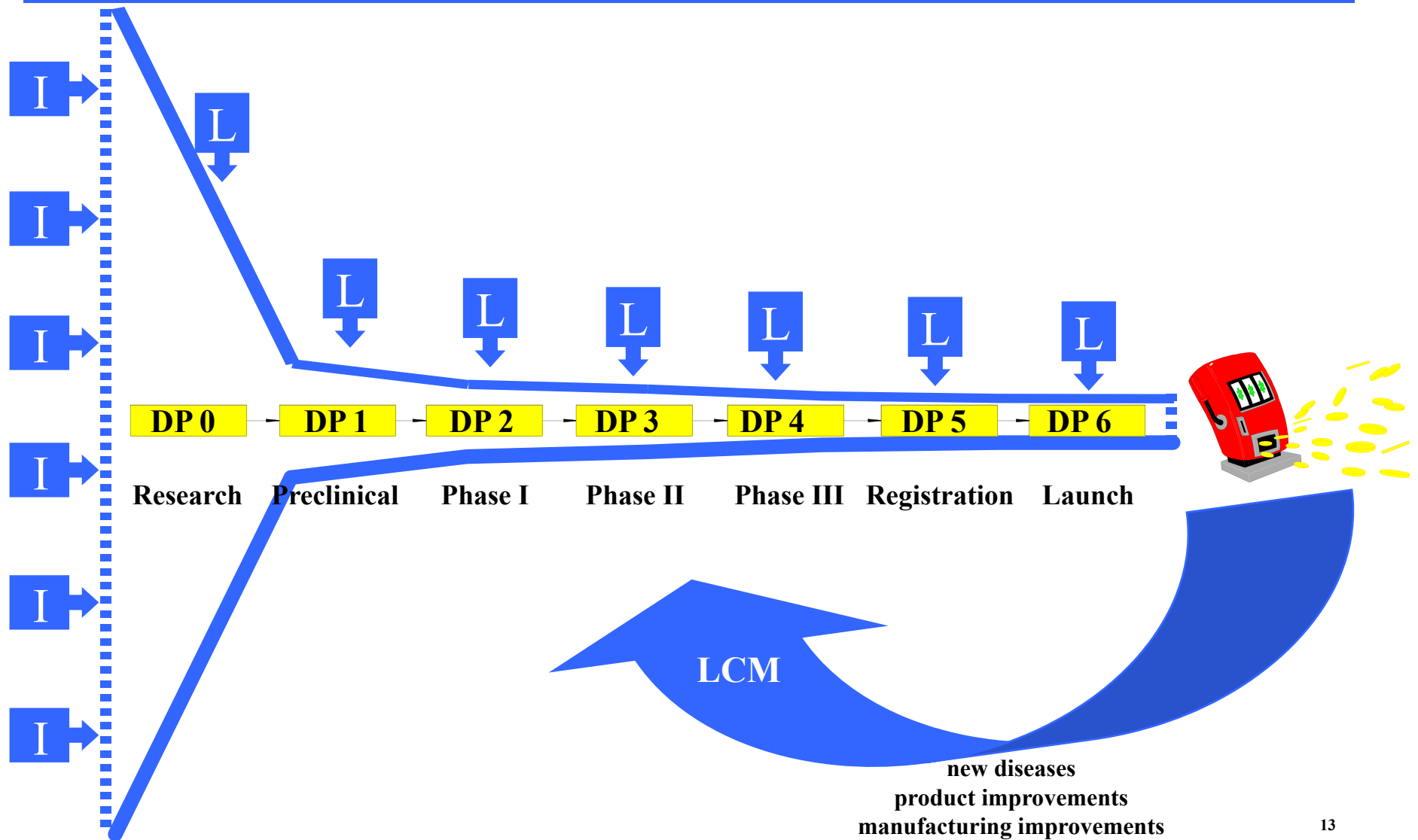
Cash flow ($ million)

Year
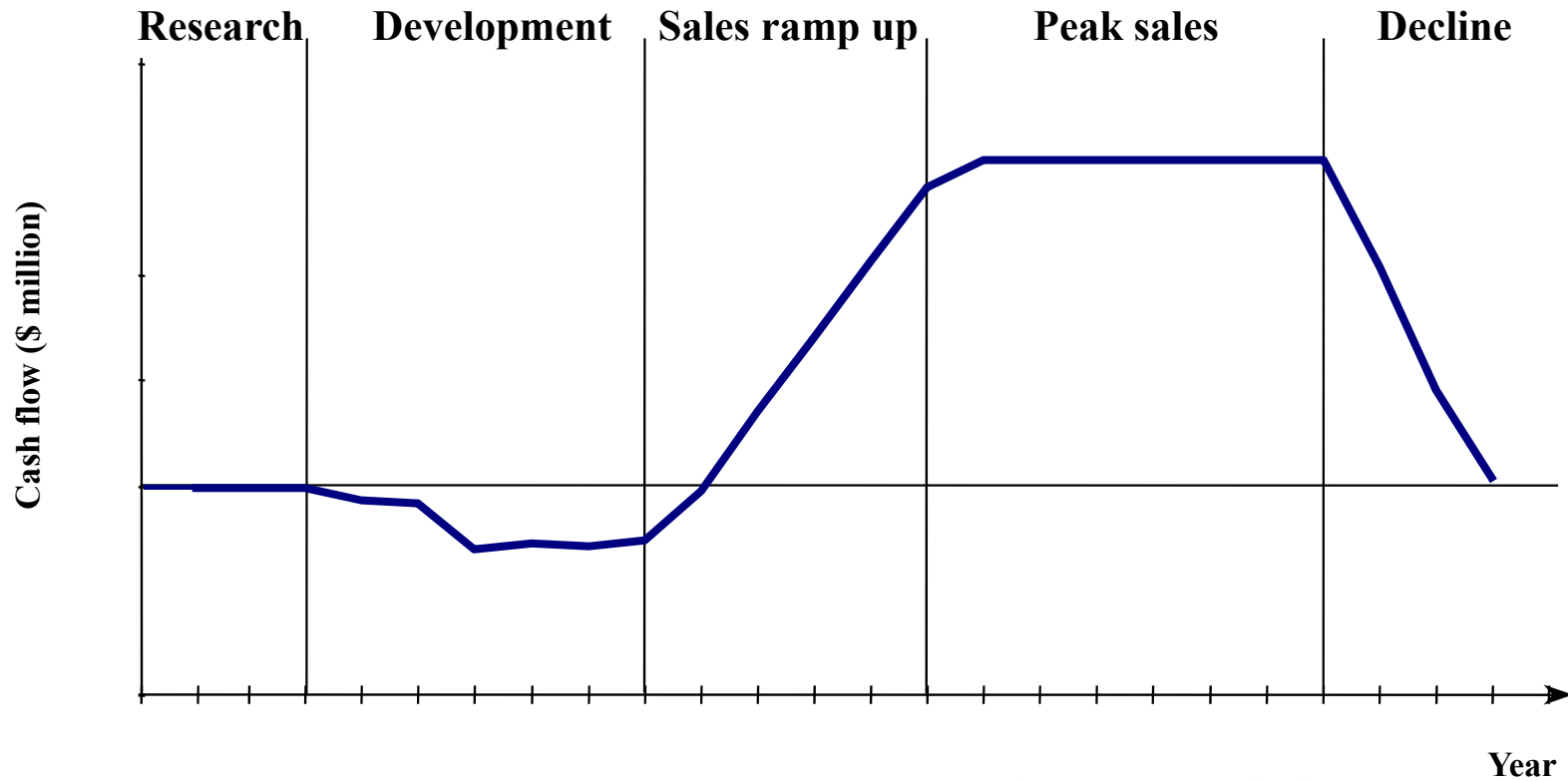
Commercial potential of a new product depends on three key factors: size of the market, our share of that market, and the price.
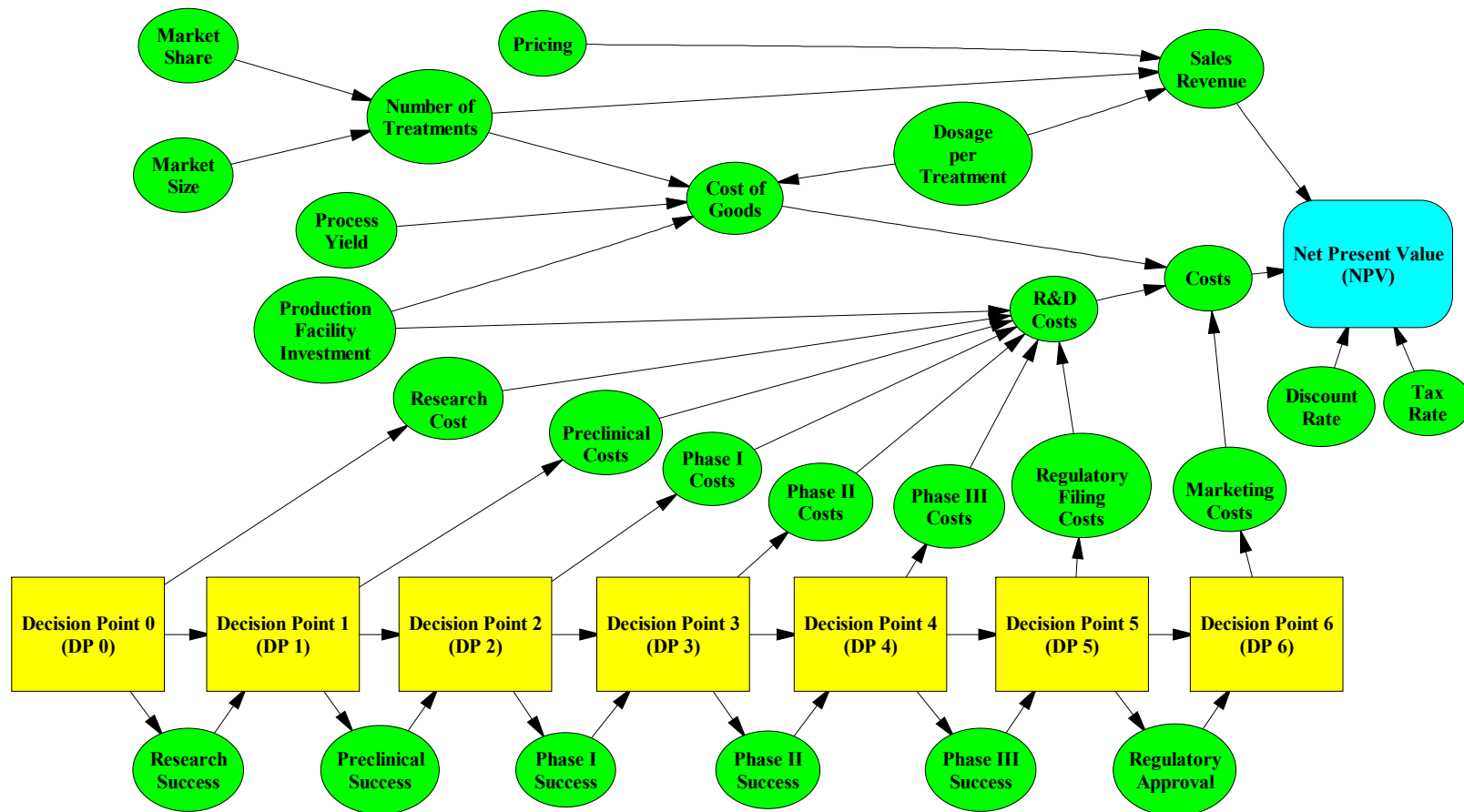
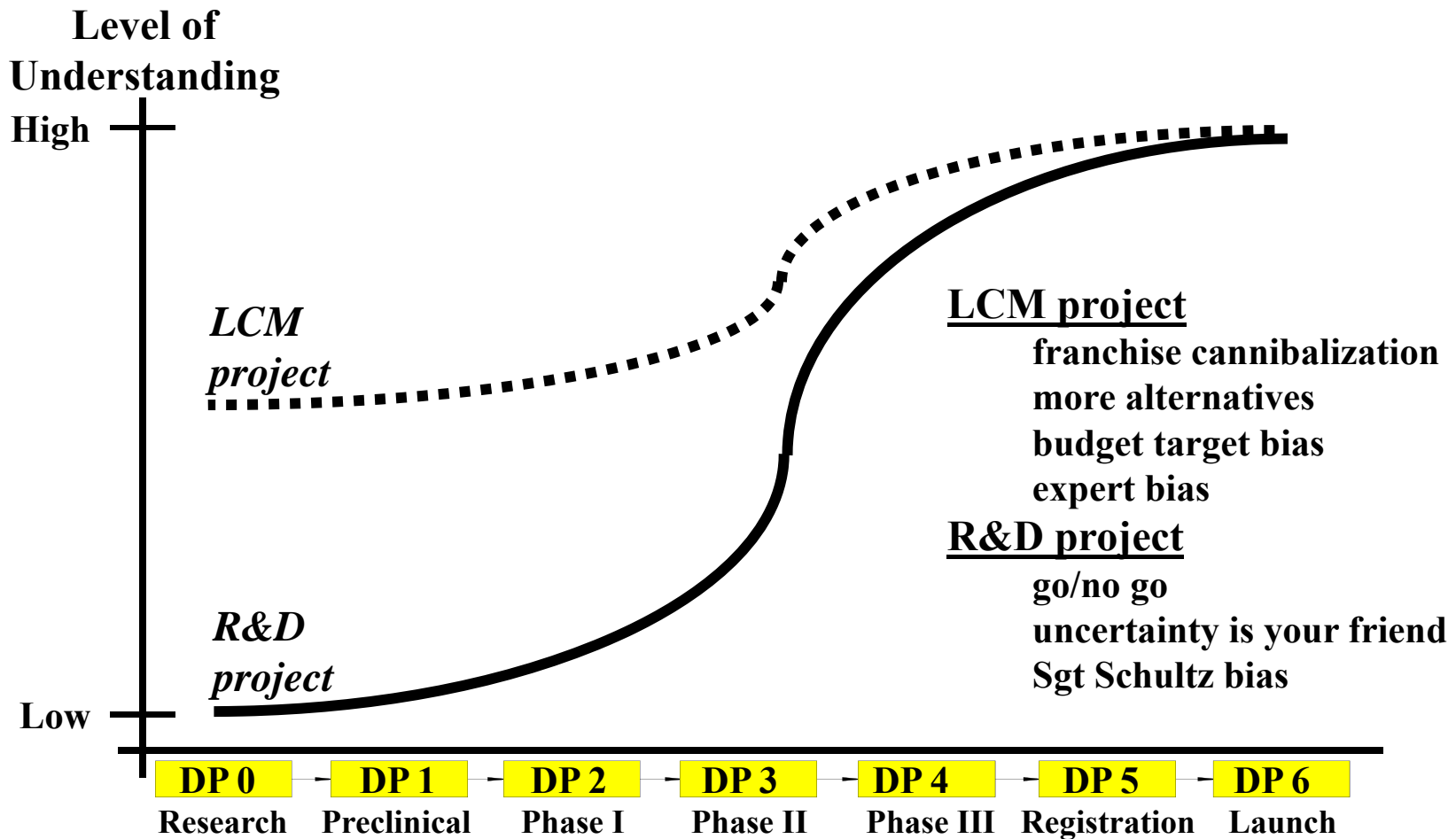*What would the influence diagram look like for a DP 2 project?*

The drug (martini) portfolio consist of R&D projects that can be internal (I) or licensed-in (L) and life-cycle management (LCM) projects.
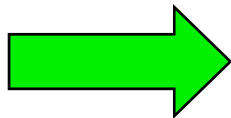

| DP 0 | DP 1 | DP 2 | DP 3 | DP 4 | DP 5 | DP 6 |

Research Preclinical Phase I Phase II Phase III Registration Launch

LCM

new diseases
product improvements
manufacturing improvements

13

"To know that we know what we know, and that we do not know what we do not know, that is true knowledge." (Confucius)

Level of Understanding

High

LCM project

R&D project

Low

LCM project
  franchise cannibalization
  more alternatives
  budget target bias
  expert bias

R&D project
  go/no go
  uncertainty is your friend
  Sgt Schultz bias

DP 0	DP 1	DP 2	DP 3	DP 4	DP 5	DP 6
Research	Preclinical	Phase I	Phase II	Phase III	Registration	Launch

AGENDA

PORTFOLIO PRIORITIZATION: THE CHALLENGE & SOLUTION
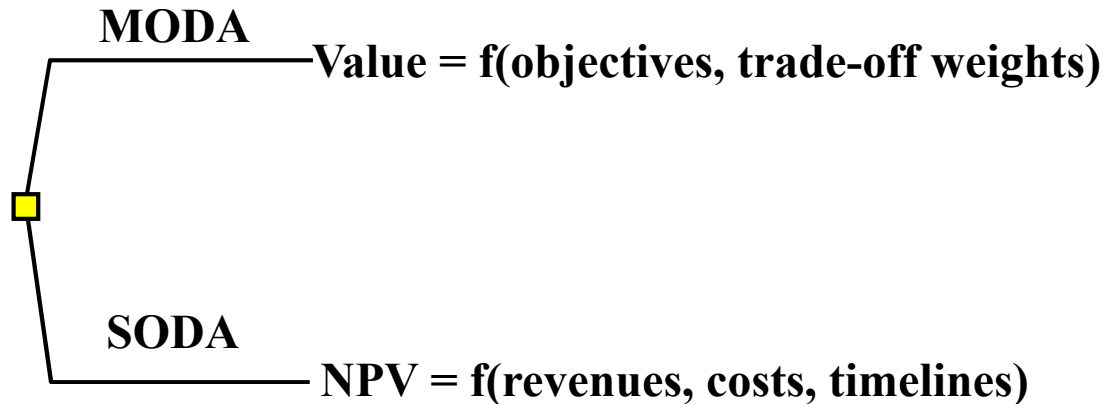
DRUG R&D DECISION-MAKING PROCESS

APPLICATION

Depending on the decision frame, we could use multi-objective decision analysis (MODA) or single-objective decision analysis (SODA).
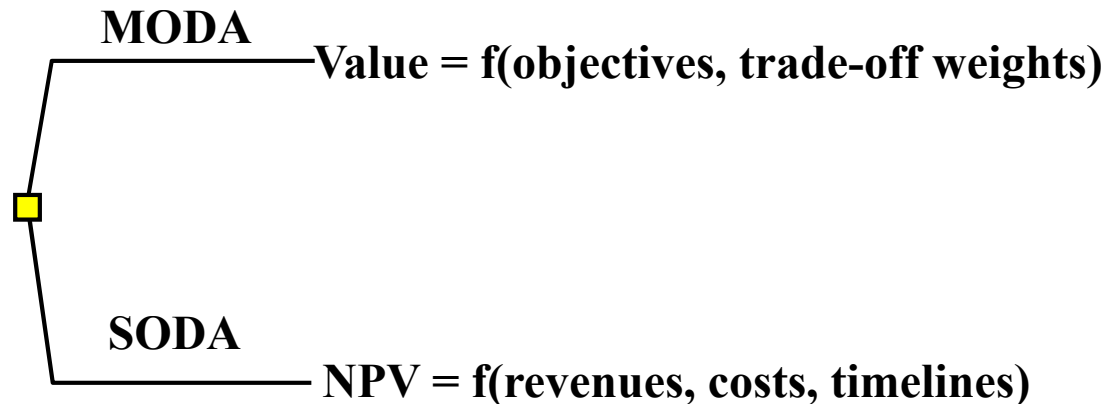
Buying a SUV

- **performance**
- **design**
- **cost**

MODA ———— **Value = f(objectives, trade-off weights)**

SODA ———— **NPV = f(revenues, costs, timelines)**

Introducing a new SUV

- **product target profile**
- **market size**
- **market share**
- **price**
- **investment**

MODA ———— **Value = f(objectives, trade-off weights)**

SODA ———— **NPV = f(revenues, costs, timelines)**

We recently used MODA to determine our research strategy where a cross-functional team first identified possible scoring criteria through brainstorming.

KEY QUESTIONS:

Is there a market?
Will it work?
Can we make it?
Can it be replaced?

Medical need
Scientific feasibility
Clinical feasibility
Clinical complexity
Preclinical success
Market channel costs
Pipeline activity
Marketed therapy
Competitive threat
Relevant animal model
Entry into market

Screening/Prioritization

Technical Feasibility	Commercial Potential

Target definition
Technical feasibility
Efficacy
Safety
Convenience
Unique selling points
Time to market
Cost per kg
Core competency
Concept feasibility/risk
Competitive alternatives

Market potential
- prevalence/incidence
- future market growth

Cost of therapy
Therapeutic need
Development effort/cost
Likelihood of replacement
Evidence for mechanistic link

The scoring criteria must be collectively exhaustive, mutually exclusive, discernible, and clearly defined.

Desirable properties for scoring criteria
> *comprehensive*, to include all important dimensions (collectively exhaustive)
> *non-redundant*, to avoid double-counting (mutually exclusive)
> *relevant*, to discriminate (test of importance)
> *well-defined*, to clearly communicate (clarity test)

Scoring must be consistent, repeatable, and defensible
> based on scorer's interpretation of the project
> not based on the scorer's interpretation of the scoring criteria

The team organized the criteria into a hierarchy of questions.

Is there a market?
Will it work?
Can we make it?
Can it be replaced?

NOTE: the top-level questions should be completely specified by the lower-level questions
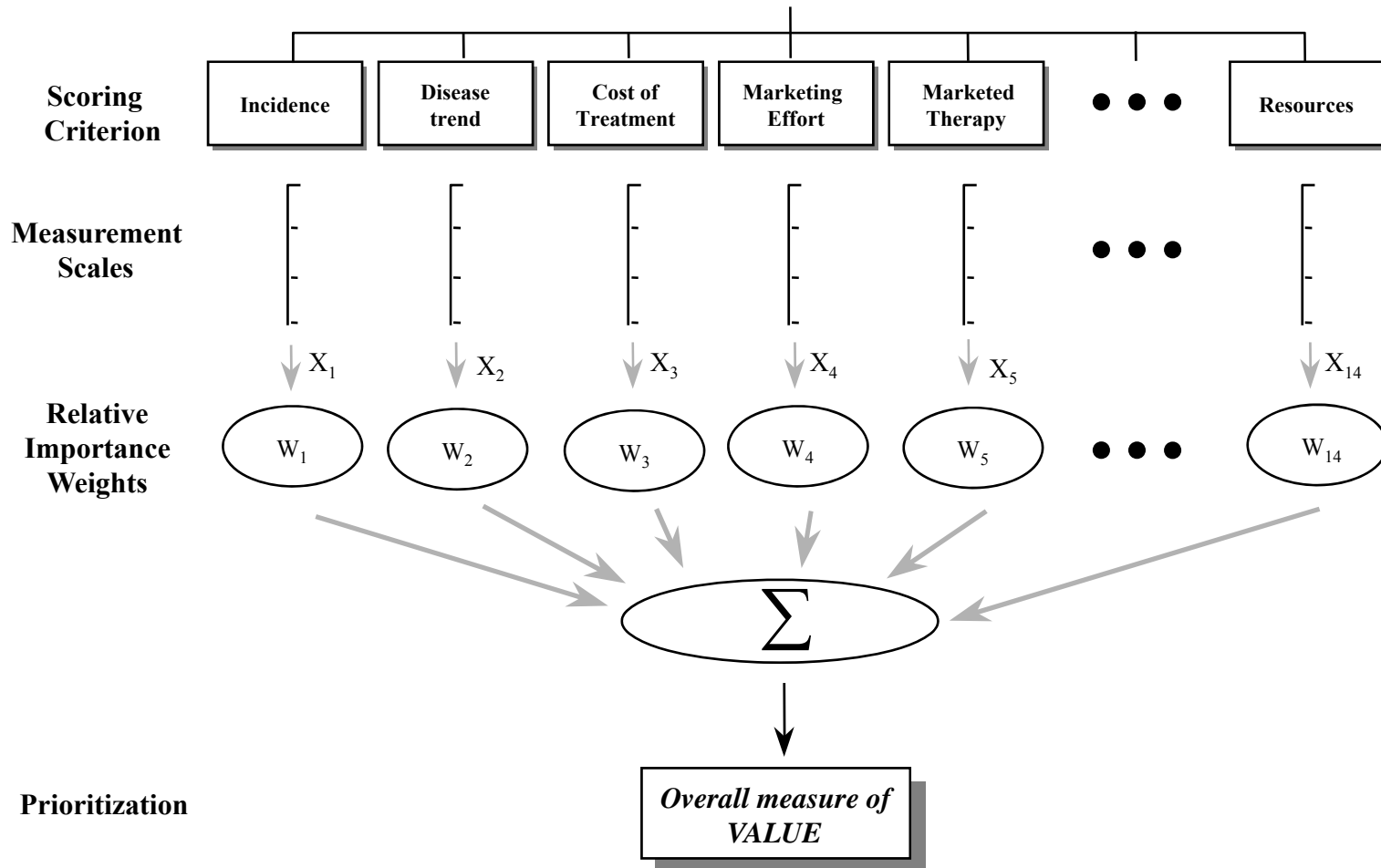
Market potential	**Competitive threat**	**Technical feasibility**	**Clinical feasibility**
Incidence/prevalence?	*Marketed therapy?*	*Target definition?*	*Efficacy?*
Disease trend?	*Pipeline activity?*	*Evidence of link?*	*Safety?*
Cost of treatment?		*Animal model?*	*Design?*
Marketing effort?		*Manufacturing capability?*	*Resources?*

The team created measurement scales for each the lower-level question where "more is better."

Market Potential	**Incidence/Prevalence**		
	Disease Trend		
	Cost of Treatment	$	<$10,000
		$ $	$10,000 - $50,000
		$ $ $	>$50,000
	Marketing Effort	X	GP or SP, new class and no experience
		X X	SP, new class or no experience
		X X X	SP, experience
Competitive Threat	**Marketed therapy**	X	Many drug options
		X X	Several drug options but unsatisfactory efficacy/safety/convenience
		X X X	Few drug options and unsatisfactory efficacy/safety/convenience
	Pipeline Activity	X	One or more compounds in Ph III
		X X	One or more compounds in Ph I/II
		X X X	Only early research or preclinical development
Technical Feasibility	**Target Definition**	X	Narrow
		XX	Medium/Variable
		XXX	Broad
	Evidence of link	X	Laboratory data
		X X	Animal model
		X X X	Clinical data
	Animal Model	X	Not available
		X X	Available, not tested
		X X X	Available, tested
	Manufacturing Capability	X	New source (non-plasma)
		X X	New plasma product or new purification technology
		X X X	Current technology
Clinical Feasibility	**Efficacy**	X	Same as current therapy
		X X	Better than current therapy
		X X X	Significantly better than current therapy
	Safety	X	Same side effects as current therapy
		X X	Moderate side effects but less than current therapy
		X X X	Minimal side effects
	Design	X	Complex trial design, not well established
		X X	Medium complexity in design and execution
		X X X	Well developed design, straightforward execution
	Resources:	X	Full blown Phase III
		X X	Combined Phase I/II or II/III with med-large patient numbers
		X X X	Combined Phase I/II or II/III with small patient numbers

The team collected primary and secondary information for 46 possible DP 0 research projects, reduced this initial set to the top-7, and then scored these.

DP 0 RESEARCH PROJECT (Disease Indication)	#1	#2	#3	#4	#5	#6	#7
MARKET POTENTIAL							
Incidence/Prevalence	~10,000	~33,000	22,000	~2,225	~50,000	~ 500	1-2%
Disease Trend	↔	↔	→	↑	↔	↑	↔
Cost of Treatment	$$$	$	$$$	$$$	$$ - $$$	$$$	$$$
Marketing Effort	X X	X X	X X X	X X X	X	X X	X X
COMPETITIVE THREAT							
Marketed Therapy	X X	X X	X X X	X X X	X (X)	X X	X X X
Pipeline Activity	X X	X (X)	X X	X X	X X	X (X)	?
TECHNICAL FEASIBILITY							
Target Definition	broad	broad	broad	med/variable	narrow	narrow	broad
Evidence of IG link	X X X	X X X	X X X	X X	X	X X X	X X X
Animal Model	X X	X	?	X X X	X X	?	X
Manufacturing Capability	X X	X X	X X	X X X	X X	X X	X X
CLINICAL FEASIBILITY							
Efficacy	X X X	X X X	X X	X X X	X X	X X X	X X X
Safety	X X X	X X X	X X X	X X X	X X X	X X X	X X X
Design	X X X	X X	X	X X X	X X	X X X	X
Resource	X X X	X	X	X X	X	X X X	X X

We never got to the next steps in MODA which are 1) assess the relative importance of the scoring criteria and 2) rank order/prioritize the indications.

Scoring Criterion

| Incidence | Disease trend | Cost of Treatment | Marketing Effort | Marketed Therapy | • • • | Resources |

Measurement Scales

X_1 X_2 X_3 X_4 X_5 X_{14}

Relative Importance Weights

W_1 W_2 W_3 W_4 W_5 • • • W_{14}

$$\Sigma$$

Prioritization

Overall measure of VALUE

Instead we relied on the "tried and true" approach in evaluating projects (R&D and LCM).

Year	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Sales in the United States								26.9	47.6	56.8	60.2	62.9	52.5	43.1	40.0	39.5	38.9	38.4	37.9	37.3	36.8	36.2
Sales in Canada								2.7	4.8	5.7	6.0	6.3	5.3	4.3	4.0	3.9	3.9	3.8	3.8	3.7	3.7	3.6
Sales in Europe									3.4	4.6	5.2	5.6	5.7	4.7	4.4	4.3	4.3	4.2	4.1	4.1	4.0	4.0
Sales in Japan										1.1	1.1	1.1	1.1	1.0	1.0	1.0	0.9	0.9	0.9	0.9	0.9	0.9
Total Sales								29.6	55.7	68.2	72.6	75.9	64.7	53.2	49.3	48.7	48.0	47.4	46.7	46.0	45.3	44.6
Rebate								2.7	5.0	6.1	6.5	6.8	5.8	4.8	4.4	4.4	4.3	4.3	4.2	4.1	4.1	4.0
Cost of goods sold								0.7	1.5	2.1	2.5	2.6	2.4	2.0	1.9	1.9	1.9	1.9	2.0	2.0	2.0	2.0
Depreciation				0.9	0.9	0.9		0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9			
Sales Force								9.0	9.0	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	4.5	4.5	4.5
Promotion & Information						7.0	7.0	23.0	23.0	11.5	11.5	11.5	11.5	11.5	11.5	11.5	11.5	11.5	11.5	2.3	2.3	2.2
Phase IV Trials									3.0	3.0	3.0											
Development Costs	3.5	3.9	4.7	8.4	8.5	8.0	7.1															
Start Up Costs			1.7																			
Operating Results (pre-tax)	-3.5	-3.9	-6.4	-8.4	-9.5	-15.9	-15.0	-6.7	13.2	37.0	40.7	46.5	36.5	26.5	23.0	22.4	21.9	21.2	20.6	33.1	32.5	31.9
Tax									5.3	14.8	16.3	18.6	14.6	10.6	9.2	9.0	8.7	8.5	8.2	13.2	13.0	12.7
Depreciation				0.9	0.9	0.9		0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9			
Change in Net Working Capital								8.9	7.8	3.8	1.3	1.0	-3.4	-3.4	-1.2	-0.2	-0.2	-0.2	-0.2	-0.2	-0.2	-0.2
New Plant Investment				14.1																		
Cash flow	-3.5	-3.9	-6.4	-22.5	-8.5	-15.0	-14.1	-14.7	1.0	19.4	24.0	27.9	26.2	20.3	15.9	14.6	14.2	13.9	13.5	20.1	19.7	19.3

NPV=   28.0

$$NPV = -3.5 - \frac{3.9}{1.07^1} - \frac{6.4}{1.07^2} - \frac{22.5}{1.07^3} - \frac{8.5}{1.07^4} - \frac{15.0}{1.07^5} - \frac{14.1}{1.07^6} - \frac{14.7}{1.07^7} + \frac{1.0}{1.07^8} + \frac{19.4}{1.07^9} + \frac{24.0}{1.07^{10}} + \cdots + \frac{19.3}{1.07^{21}} \approx 28.0$$
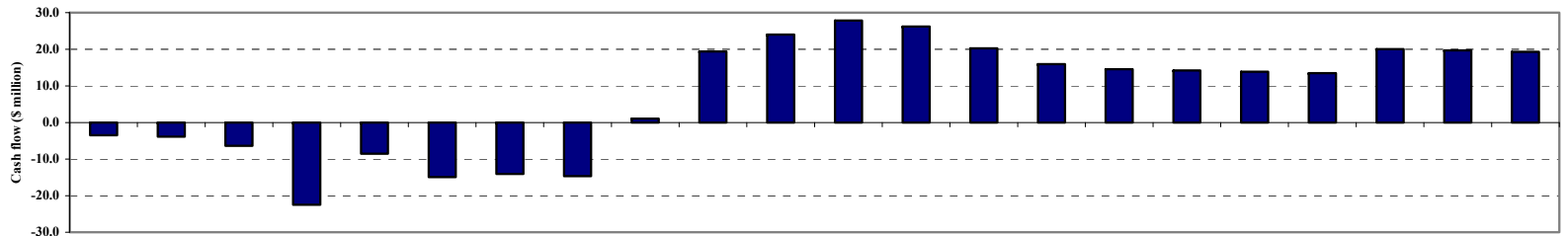
For each project, we varied the inputs in the decision-focused model and generated various outputs.
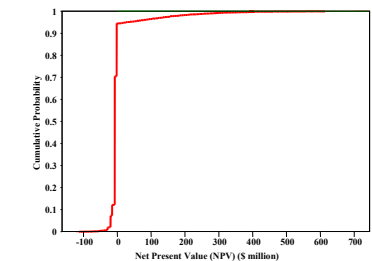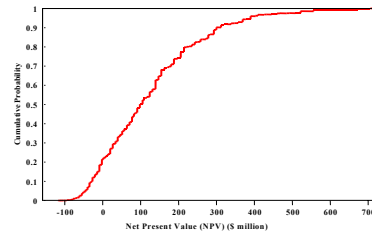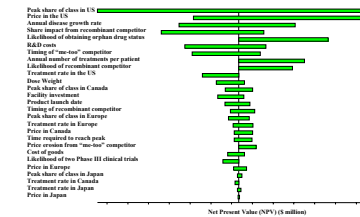
INPUTS

OUTPUTS

Peak sales = 150

Base-Case NPV = 140

Commercial Value = 125

Expected NPV = 15

ROI = 3.8

The portfolio prioritization problem is finding the right static balance between R&D projects and life-cycle management (LCM) projects in a dynamic and operational environment.

| Project ID	DP	new R&D	LCM	Peak Sales	CV	EV	Investment	ROI	recency
BAY 10-5233	4	yes		280	260	155	55	6.4	2000
BAY 19-8512	1		yes	40	80	60	20	5.7	2000
BAY 19-8513	1		yes	10	15	10	10	2.9	2000
BAY 19-8514	1		yes	15	10	5	15	2.0	2000
BAY 19-8515	1		yes	10	40	30	15	4.1	2000
BAY 41-1000	5		yes	550	370	335	35	13.3	2000
BAY 50-4798	1	yes		225	240	40	55	6.3	1998
BAY 57-9602	1	yes		150	125	15	60	3.8	1999

Research
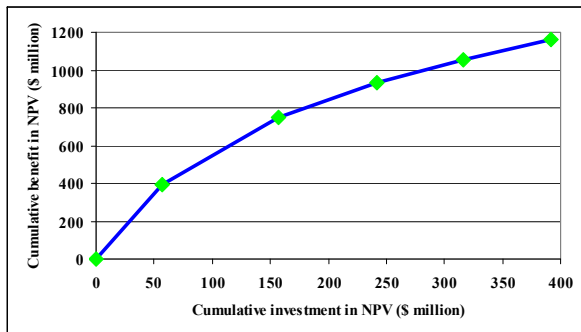
Preclinical Development
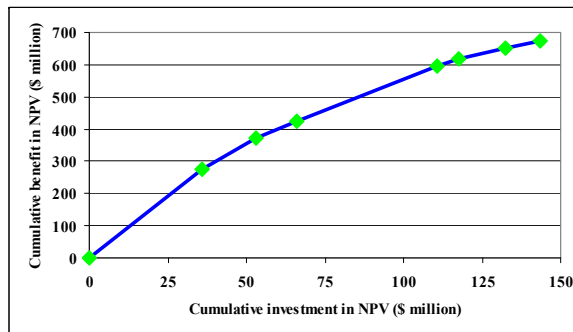
Clinical Development
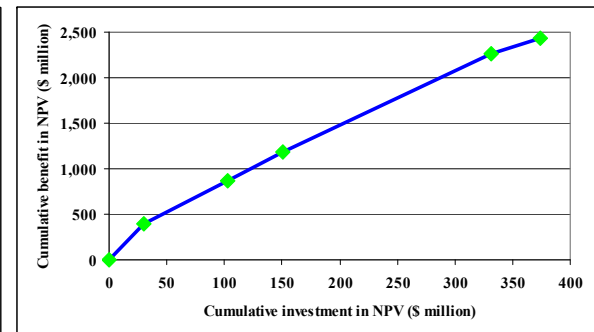
Size depends on attrition and budget

"He who learns but does not think is lost. He who thinks but does not learn is in great danger." (Confucius).

JOURNALS/PERIODICALS

Management Science
Interfaces
Operations Research
IEEE Transactions on Engineering Management
IEEE Transactions on Systems, Man, and Cybernetics
Journal of the Operational Research Society
European Journal of Operations Research
Research•Technology Management
Decision Sciences
Decision Support Systems
Harvard Business Review
Sloan Management Review
Organizational Behavior and Human Decision Processes
Journal of Behavioral Decision Making
Behavioral Science
Acta Psychologica
Psychological Bulletin
Annual Review of Psychology
Risk Analysis
Reliability Engineering and System Safety
Long Range Planning
Technology Forecasting and Social Change
Journal of Management Studies
Journal of Science Policy and Research Management
Journal of Multi-Criteria Decision Making
Science
Medical Decision Making
Drug Information Journal
Drug Discovery Today
In VIVO
Energy and Technology Review
Pipeline and Gas
Nuclear Technology
Environment Management

BOOKS

Introduction to Decision Analysis by David C. Skinner, Probabilistic Publishing, 1999.

Making Hard Decisions: An Introduction to Decision Analysis by Bob Clemen, Duxbury Press, 1996.

Strategic Decision Making: Multiobjective Decision Analysis with Spreadsheets by Craig Kirkwood, Duxbury Press, 1997.

Smart Choices: A Practical Guide to Making Better Decisions by John Hammond, Ralph Keeney, and Howard Raiffa, Harvard Business Press, 1999.

The Smart Organization: Creating Value through Strategic R&D by David Matheson and Jim Matheson, Harvard Business Press, 1998.

Value-Focused Thinking: A Path to Creative Decisionmaking by Ralph Keeney, Harvard Business Press, 1992.

Portfolio Management for New Products by Robert Cooper, Scott Edgett, and Elko Kleinschmidt, Addison Wesley, 1998.

Decision Analysis with Supertree by Peter McNamee and John Celona, Scientific Press, 1990.

Decision Traps: The Ten Barriers to Brilliant Decision-Making and How to Overcome Them by J. Edward Russo and Paul Schoemaker, Simon & Schuster, 1989.