RevAssist® & *S.T.E.P.S.*®
Risk Management Strategies

Experience and Perspective

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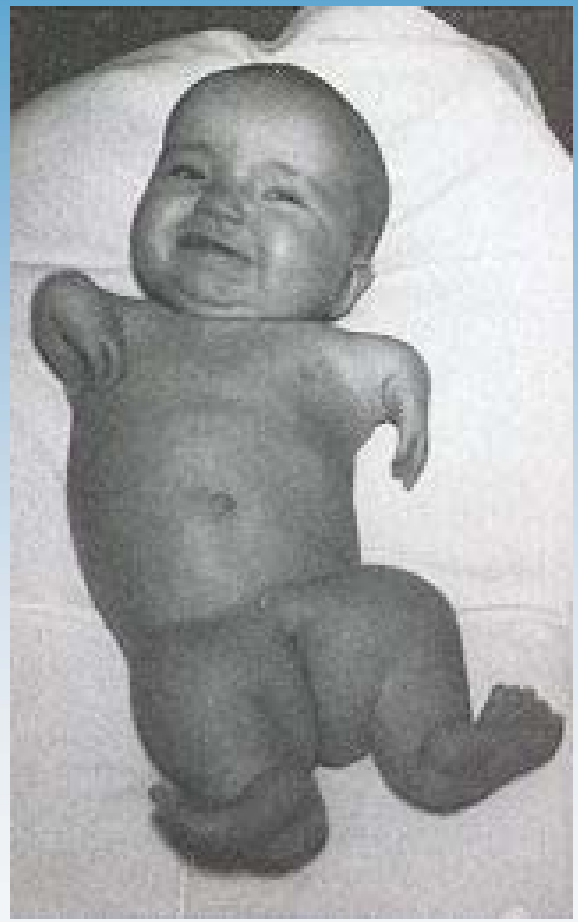
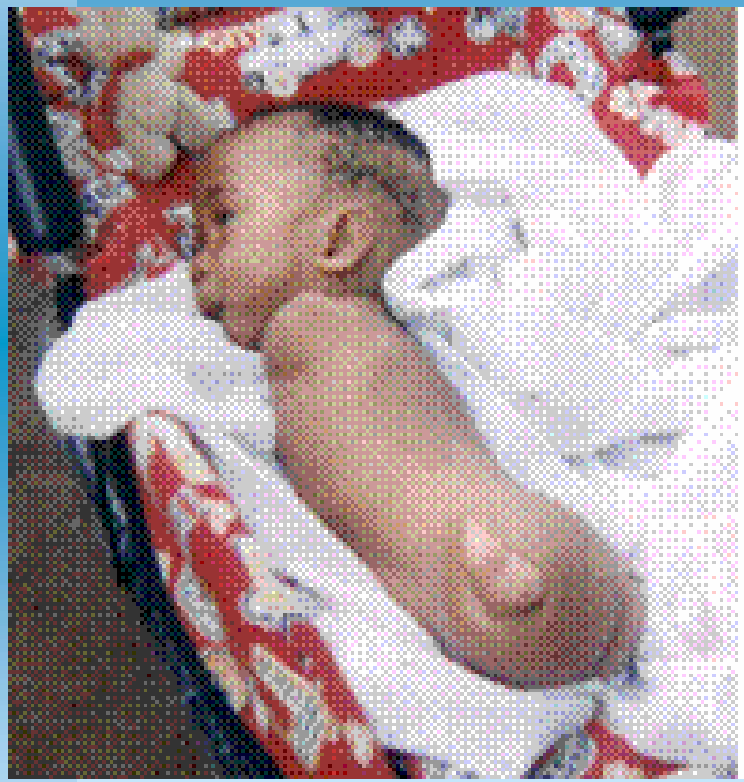
Thalidomide – Germany 1960



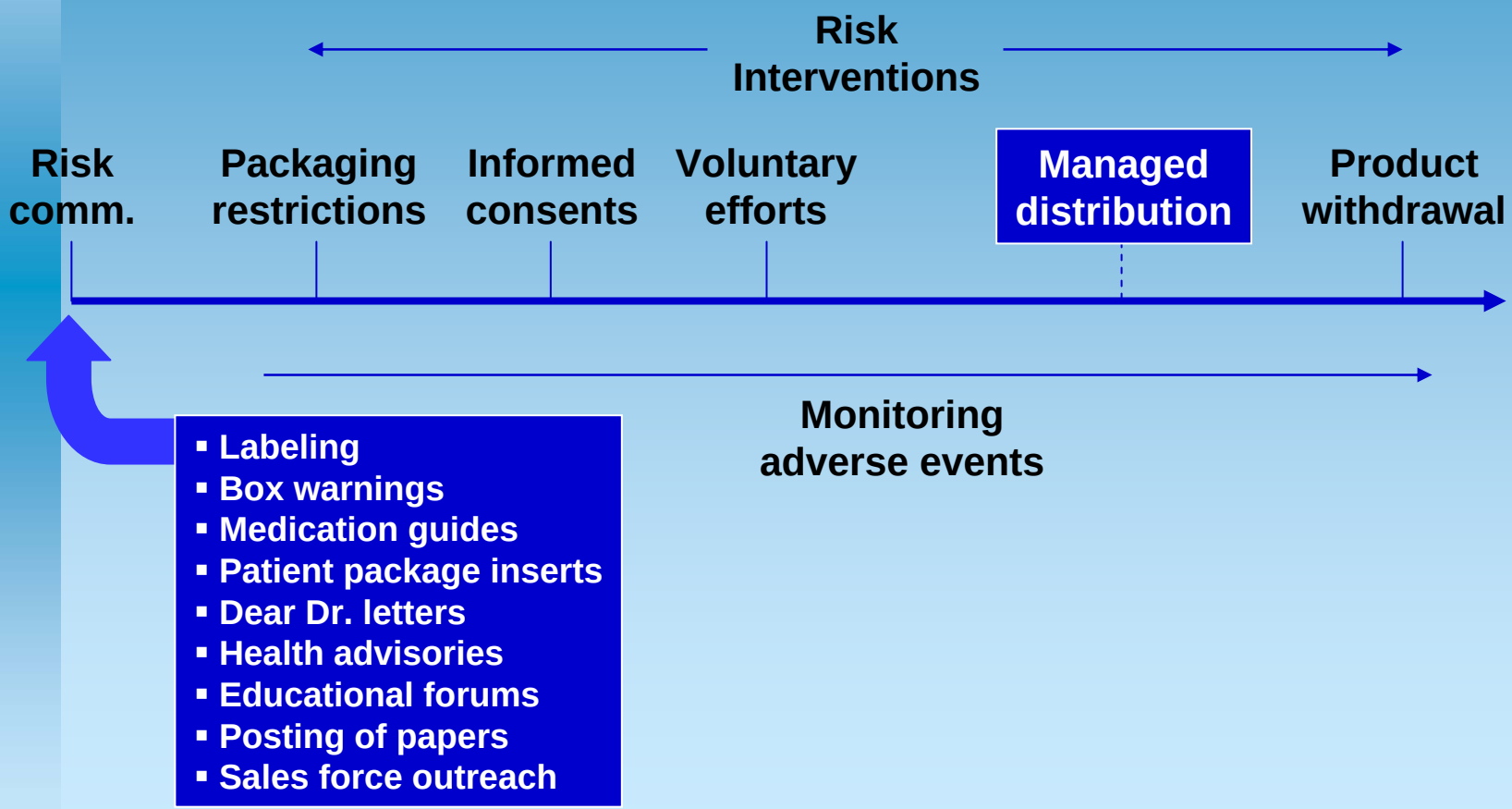
Thalidomide – Uganda & Brazil 2005



Presentation Overview

- **RevAssist® & *S.T.E.P.S.*® RiskMAPs**
  - **Objectives**
  - **Operation**
  - **Ensuring effectiveness**
- **Key operating metrics**
  - **Enrolment & prescription volume**
  - **Outcomes & effectiveness**
- **Upsides / Downsides**
- **Celgene experience & perspective**

Risk Management Options



Adopted RiskMAP Programs

S.T.E.P.S.®

System for Thalidomide Education and Prescribing Safety

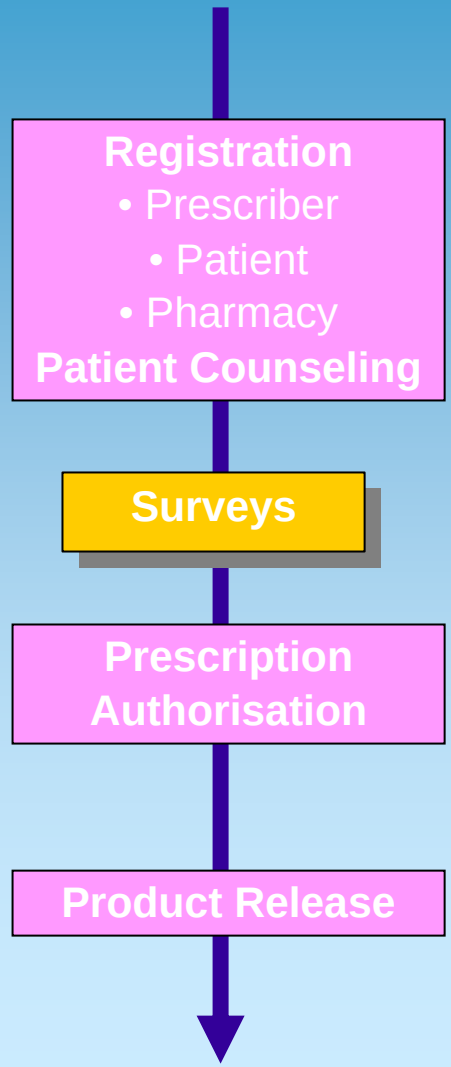
RevAssist®

RevAssist® program for Revlimid education and prescribing safety

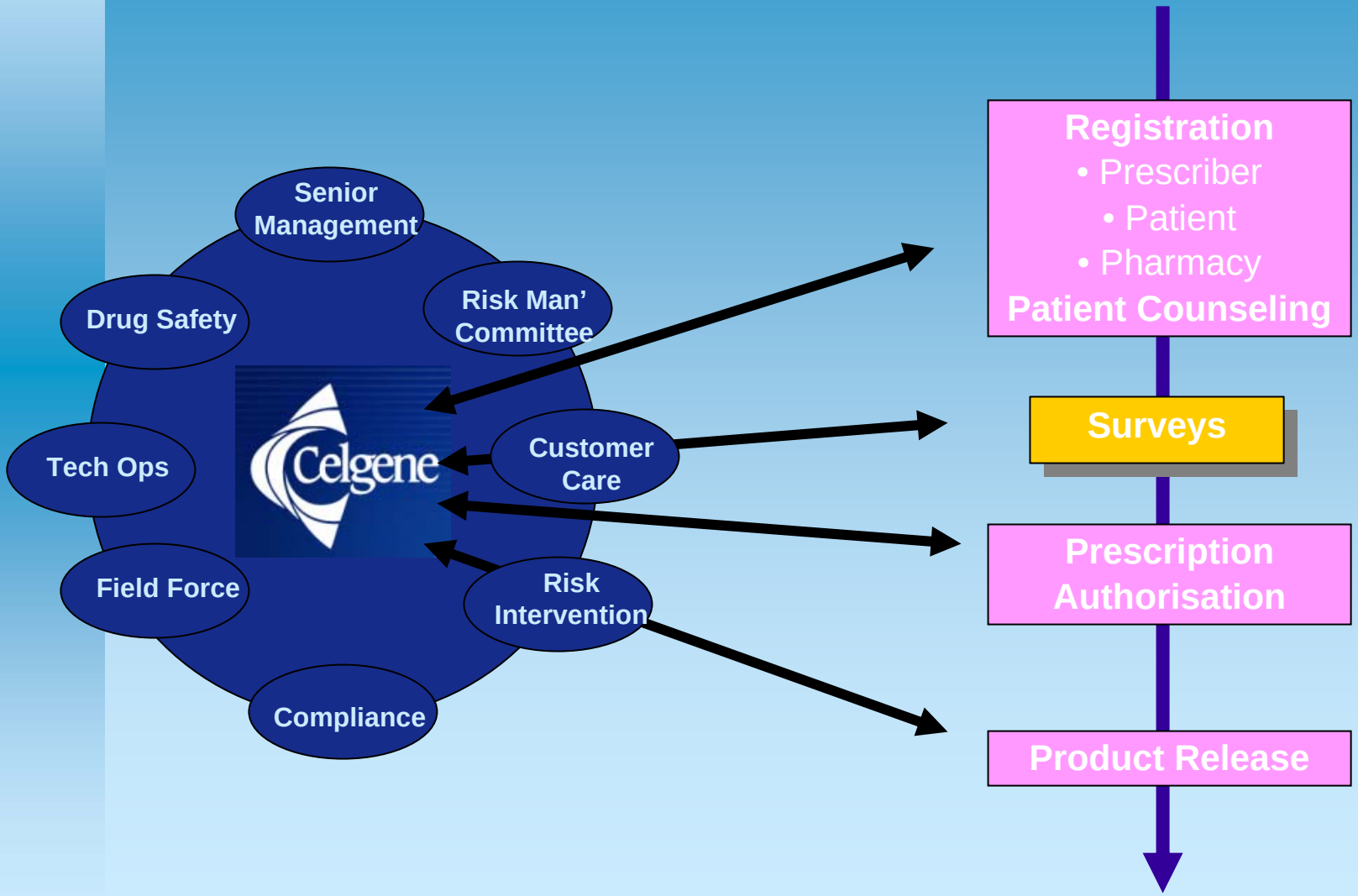
RiskMAP Overview

- **Goals:**
  - **Avoid fetal exposure**
  - **Manage cytopenias (RevAssist® only)**
- **Components of *S.T.E.P.S.*® and RevAssist ® risk management programs:**
  - **Education**
    - **Physicians, nurses and pharmacists**
    - **Patients**
  - **Active risk aversion**
  - **Controlled, performance linked distribution**

S.T.E.P.S.® & RevAssist® Overview



S.T.E.P.S.® & RevAssist® Overview



RiskMAP operation:
Patient Risk Classifications

- **Six Risk Classifications**
- **Six Patient/Physician Agreement Forms (PPAF)**
  - **Female (4)**
    - **Adult female of child-bearing potential**
    - **Adult female not of child-bearing potential**
    - **Female child of child-bearing potential**
    - **Female child not of child-bearing potential**
  - **Male (2)**
    - **Adult Male**
    - **Male Child**
- **Risk Classification drives program components and risk intervention measures**

RiskMAP operation:
Pregnancy Prevention

- **FCBP (Females of Childbearing Potential) must**
  - **completely abstain from sexual intercourse, OR**
  - **use 2 methods of "effective birth control" simultaneously for**
    - **4 weeks before the therapy**
    - **during therapy**
    - **during therapy interruptions**
    - **4 weeks after completion of therapy**
- **Male**
  - **Use a latex condom, during any sexual contact with females of childbearing potential even if he has undergone a successful vasectomy**

RiskMAP operation:
Pregnancy testing

For Females of Child Bearing Potential (FCBP)

- **Before therapy**
- **During Therapy**
- **Pregnancy testing during therapy interruptions**
- **4 weeks after completion of therapy**

RiskMAP operation:
Restricted Prescriptions

- Prescribe No More Than 4 weeks (28 days)
- No automatic refills
- Patient and Physician should complete and sign Patient-Physician Agreement Form for each initial prescription
- Counseling not to share drug, not to donate blood or sperm

Measuring effectiveness:
Prescriber and Patient Surveys

Females of child bearing potential

	Initial prescription	Repeat prescription
Prescriber	■ Pregnancy test ■ Dose & duration	■ Patient counseling ■ Change in patient fertility status
Patient	■ Sexual activity ■ Contraception compliance ■ Pregnancy status	■ Sexual activity ■ Contraception compliance ■ Pregnancy status ■ Drug sharing ■ Blood donation ■ Fertility status

Key Operating Metrics:
Use from Launch to Dec 31st 2006

	S.T.E.P.S.®
Program Registration	**> 36,000 pharmacies** **> 20,000 prescribers** **> 136,000 patients**
Prescriptions	**> 880,000 prescriptions**

Key Operating Metrics : *S.T.E.P.S.*®

Launch to date

No in utero exposure resulting in congenital malformations associated with thalidomide in over one million prescription cycles.

Key Operating Metrics : RevAssist ®

Launch to 31 Dec 2006

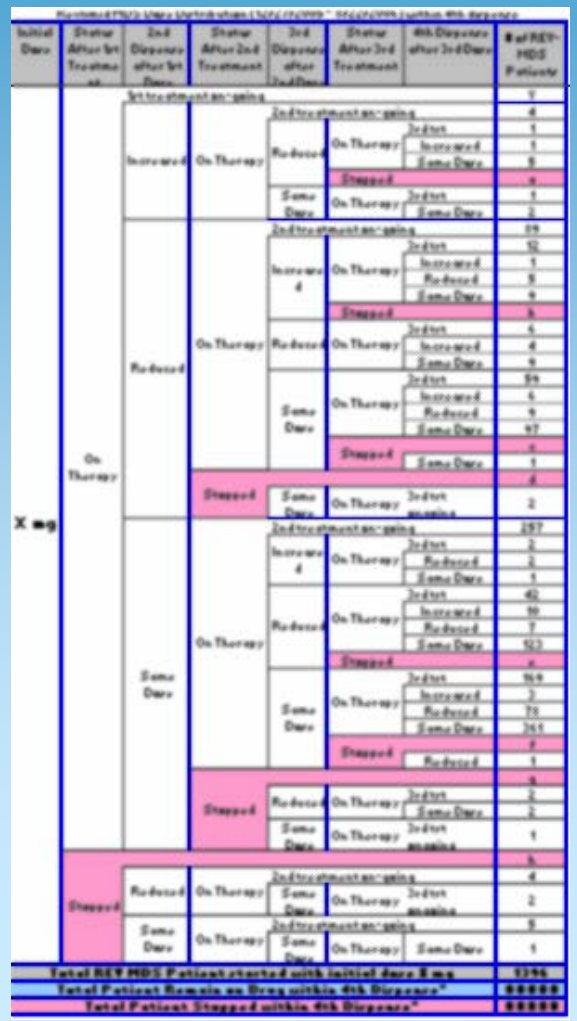
Patient survey data indicates a high level of understanding of program objectives

Knowledge Questions	Period Ending 26 Jun 2006		Period Ending 26 Dec 2006	
	FCBP N (%)	Males N (%)	FCBP N (%)	Males N (%)
No. of Respondents	34	264	93	759
Women should not get pregnant while taking Revlimid	34 (100)	NA	91 (97.8)	NA
Revlimid may cause birth defects	34 (100)	259 (98.1)	91 (97.8)	739 (97.4)
Women who could get pregnant need to use two different types of birth control	34 (100)	NA	89 (95.7)	NA
Birth control pills cannot be used alone to prevent pregnancy while taking Revlimid	34 (100)	NA	90 (96.8)	NA
It is important to stop taking Revlimid before trying to get pregnant	34 (100)	259 (98.1)	90 (96.8)	736 (97.0)

Upsides :
Drug Utilization & Exposure Data

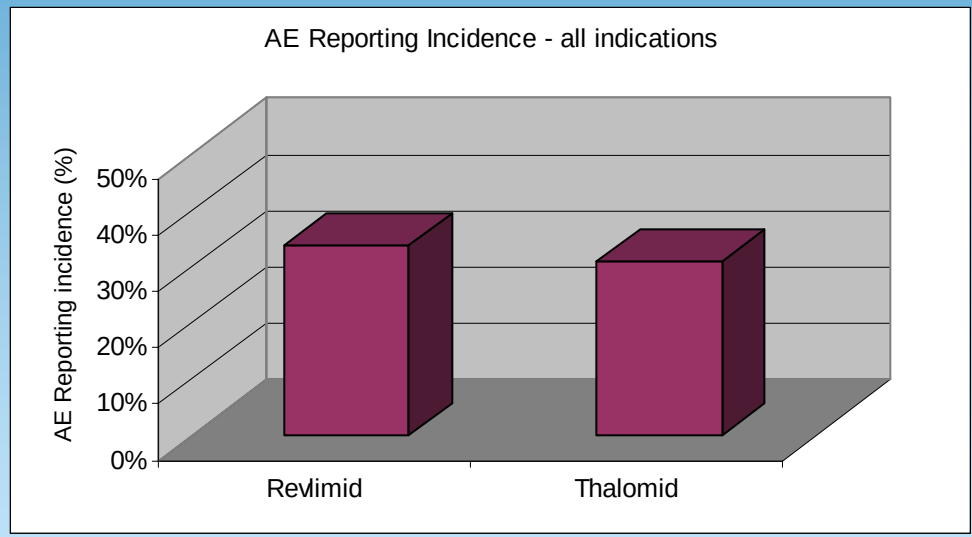
Precise product usage data:

- Dose adjustments
- Drug withdrawals
- Drug interruptions
- Usage vs approved dose
- Indication information



Upsides : Adverse Event reporting

- Multiple, defined points of contact with prescribers, pharmacies and patients drives higher AE reporting rates
- Treatment discontinuations permit investigation of cause
- Individual patient experience may be tracked via social security number (or other unique patient identifier)



Impact :

Healthcare providers, Patients & Industry.

- **Average monthly call volume: 26,000**
- **Average daily call volume: 1300**
- **Average daily fax volume: 1400**
- **Average monthly survey volume: 18,800**

Celgene experience & perspective

- Highly effective risk minimisation via controlled distribution is possible.
- Considerable burden on healthcare providers, dispensers & patients.
- Effective risk minimisation requires considerable industry expertise and resolve – an engrained culture of risk management, central to the company's philosophy & values.
- RiskMAPs must be proportionate to the perceived level of risk.

Celgene experience & perspective

- It should be possible to adjust RiskMAP methods and emphasis based on risk variation across patient sub-groups.
- Controlled distribution RiskMAPs should permit easement of some aspects of drug regulation compared with conventionally distributed products.
- These programs evolve with practical experience necessitating ongoing refinement – guidance is needed on change approval. Minor adjustments to RiskMAP programs should not be subject to prior regulatory approval.