About OMICS International

OMICS International through its Open Access Initiative is committed to make genuine and reliable contributions to the scientific community. OMICS International hosts over 700 leading-edge peer-reviewed **Open Access Journals** and organizes over 1000+ **International Conferences** annually all over the world. OMICS International journals have over 3 million readers and the fame and success of the same can be attributed to the strong editorial board which contains over 50000 About OMICS International eminent personalities that ensure a rapid, quality and quick review process. OMICS International signed an agreement with more than 1000 **International Societies** to make healthcare information Open Access. OMICS International Conferences make the perfect platform for global networking as it brings together renowned speakers and scientists across the globe to a most exciting and memorable scientific event filled with much enlightening interactive sessions, world class exhibitions and poster presentations.



Non-compliance, Misconduct and Fraud



Rucha Majmundar Mehta
GCP Auditor
Clinical Research Conference 2015
Orlando - FL

Horror Stories in Scientific Research do not always start and end with Fraud but includes mishaps and misconducts at the level of the Sponsor, Investigators and IRB/IEC

Clinical Quest

Fraud Associated Characters

- Incompetence
- Arrogance
- Greed
- Ambition
- Laziness
- Dishonesty
- Bad Science
- Poor Ethics
- Contempt for Patients
- Contempt for Rules
- Contempt for sponsor
- Poor team spirit

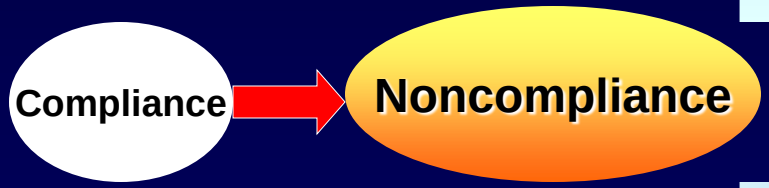
COMPLIANCE IN CLINICAL TRIALS



THE NON COMPLIANCE CONTINUUM



DRIVERS OF NON COMPLIANCE



Honest Error

- Failure to see the "experiment"
- Complicated study procedures
- Poor infrastructure
- Miscalculation/ misjudgment

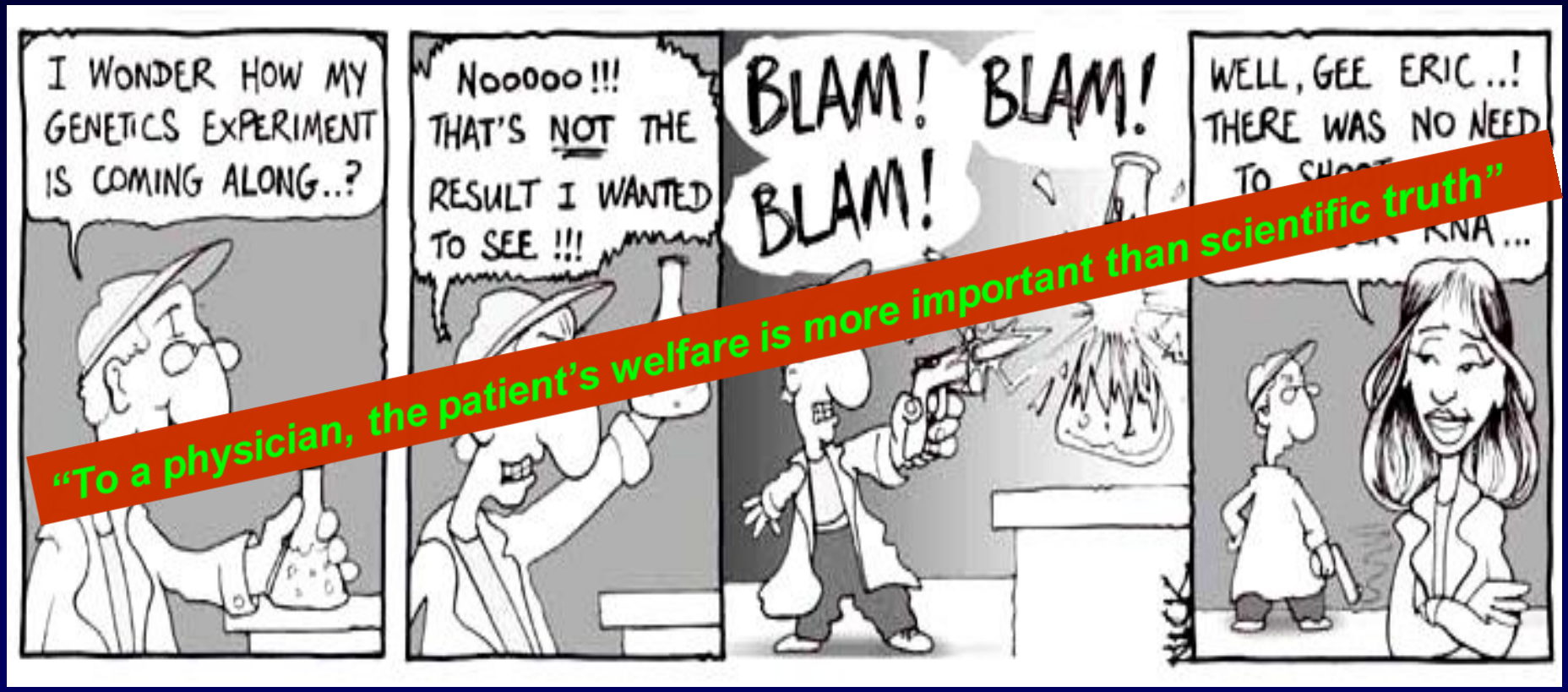
Difference of opinion

- Study protocol ambiguous
- Rationale of study unclear
- Patient inconvenience
- Overrated techniques/ equip.

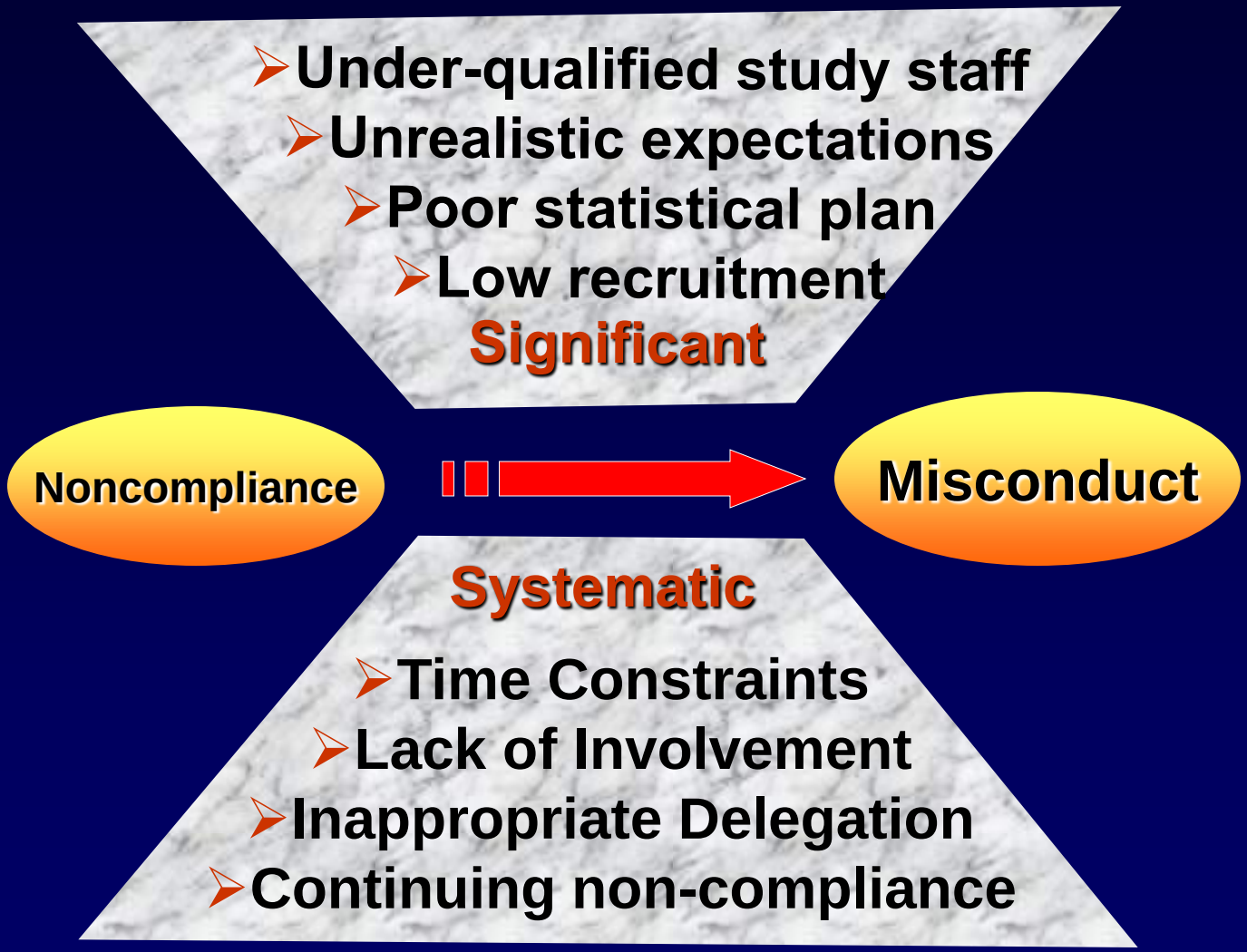
Non-compliance: GCP demands that you say NO!

MISCONDUCT

Pre-conceived notions



MAJOR DRIVERS OF MISCONDUCT



EXAMPLES OF SCIENTIFIC MISCONDUCT



Source data as uncertified photocopies

Patients not dating their own ICF's

Direct CRF entry

Misconduct

Source Data withheld

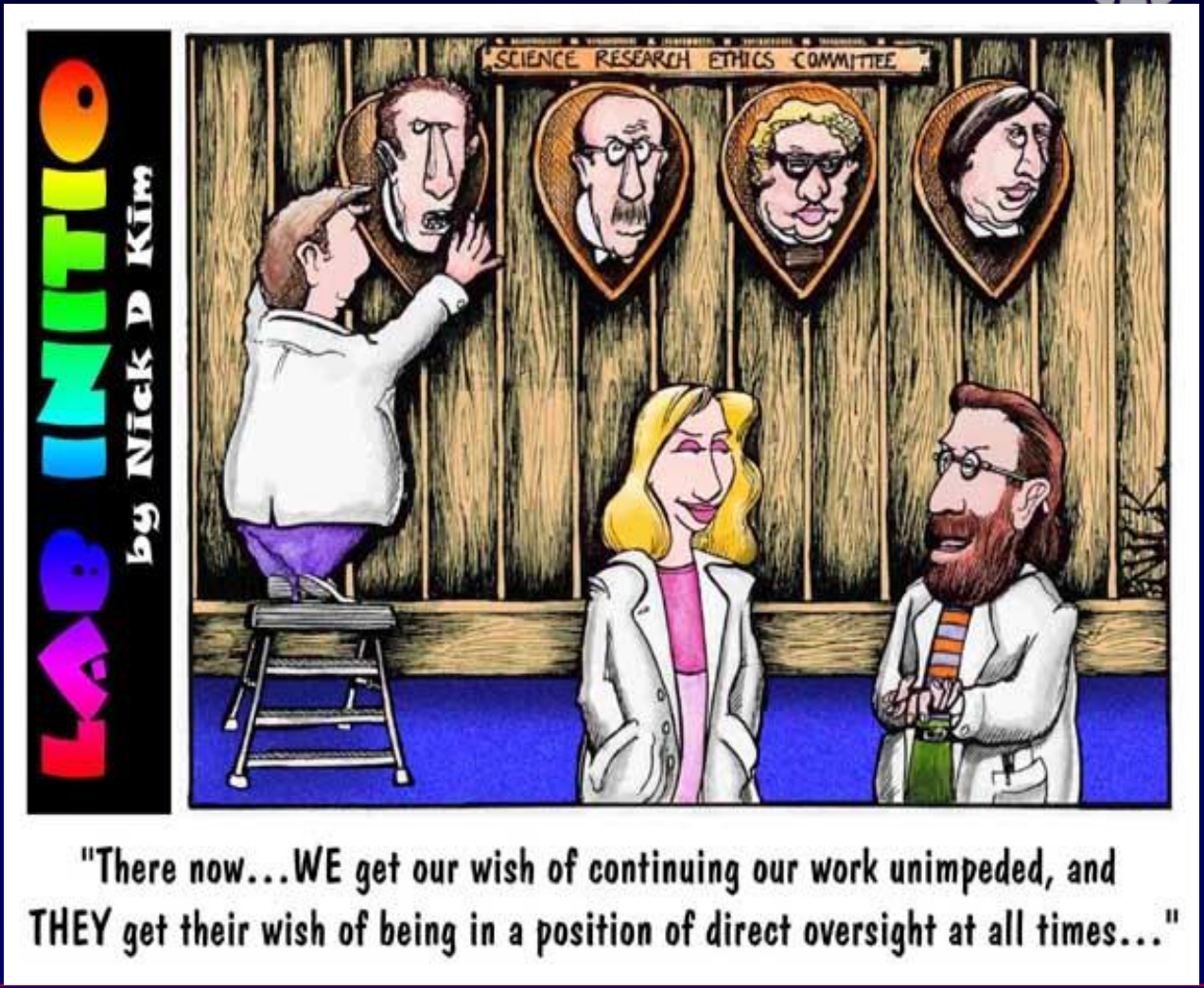
Under reporting Adverse Events

Unexplained handwritten changes to CRF and Source Data

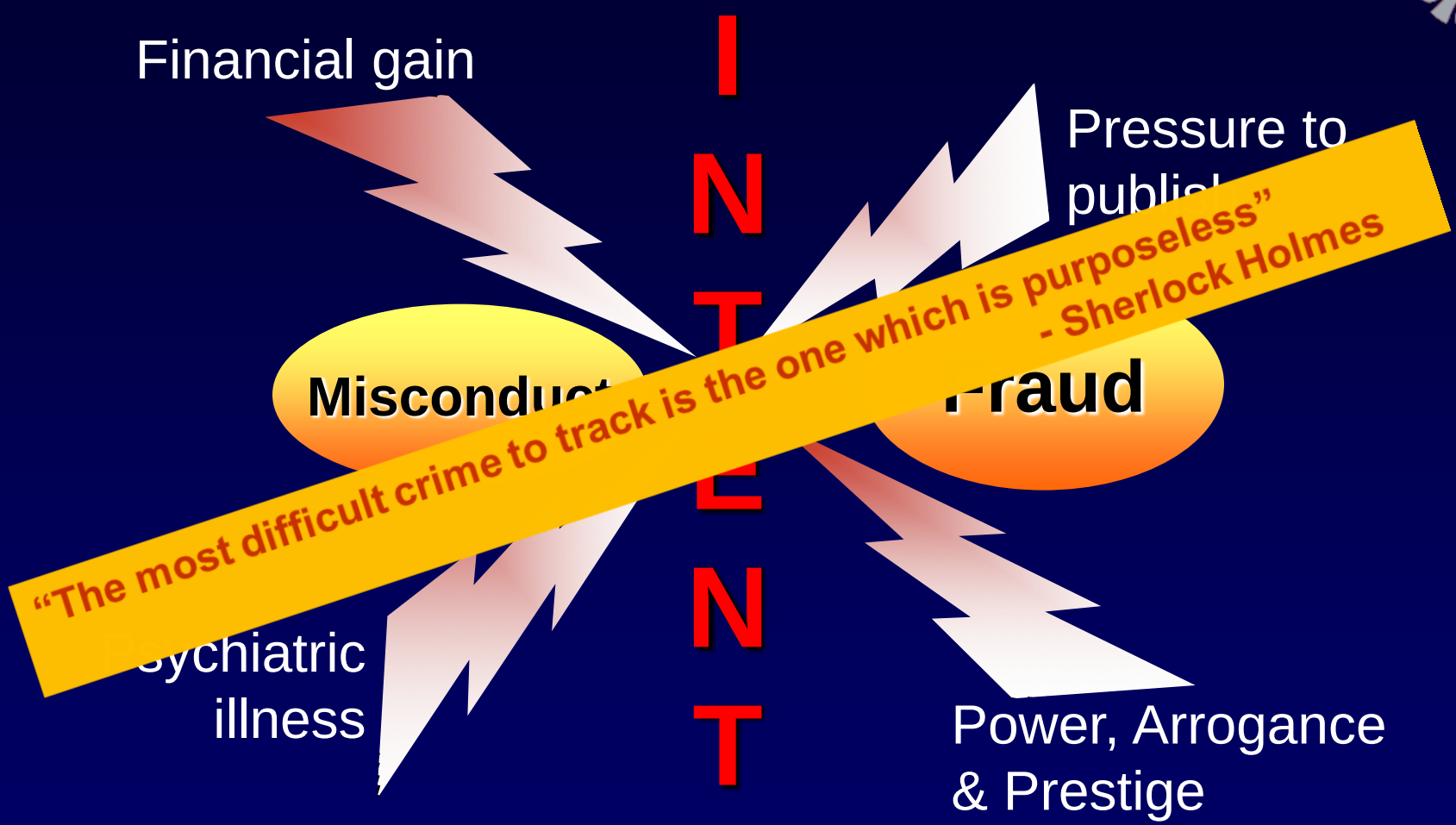
FRAUD

‘‘Scientists aren’t saints. The field is so competitive that many misbehave in many ways; few falsify results.’’

-David Goodstein



DRIVERS OF FRAUD



INCIDENCE OF FRAUD

Believed to be uncommon

Estimated to be 4-5% annually

No systematic registration
(except UK, Denmark & USA)



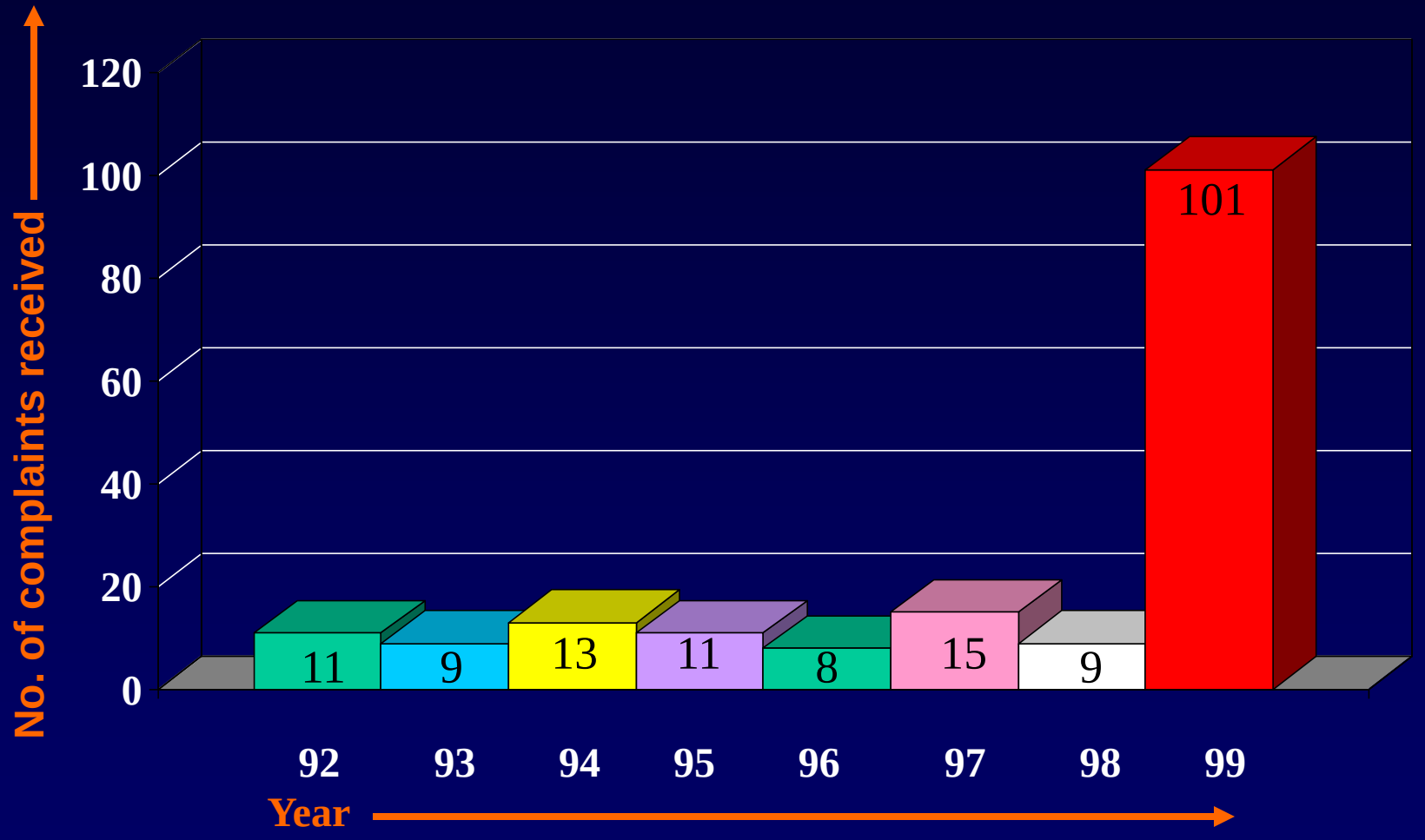
"We believe probabilities and choose the most likely. This is very scientific use of imagination"

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"I am going to enter you as three patients, in your name, nee name and pseudonym."

COMPLAINTS LODGED AT THE US FDA



The incidence of reporting fraud is on the increase

Falsification of Data

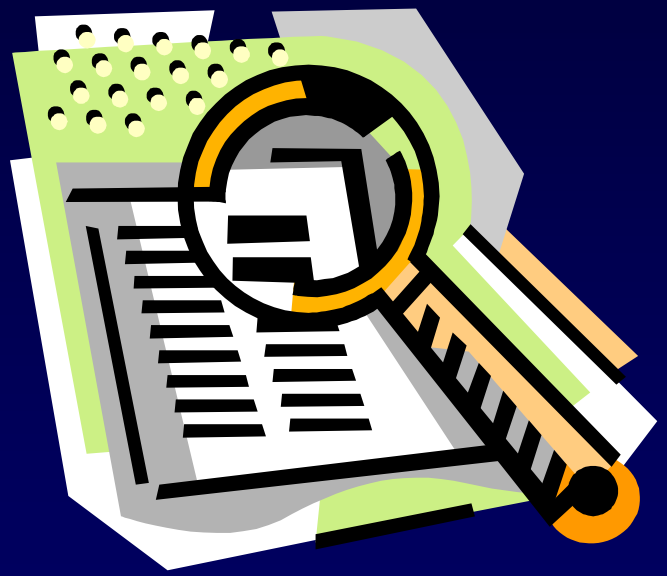
- Falsification of data includes
  - creating, altering, recording, or omitting data in such a way that the data do not represent what actually occurred

Examples of falsification of data include but are not limited to

- creating data that were never obtained;
- altering data that were obtained by substituting different data;
- recording or obtaining data from a specimen, sample or test whose origin is not accurately described or in a way that does not accurately reflect the data
- omitting data that were obtained and ordinarily would be recorded

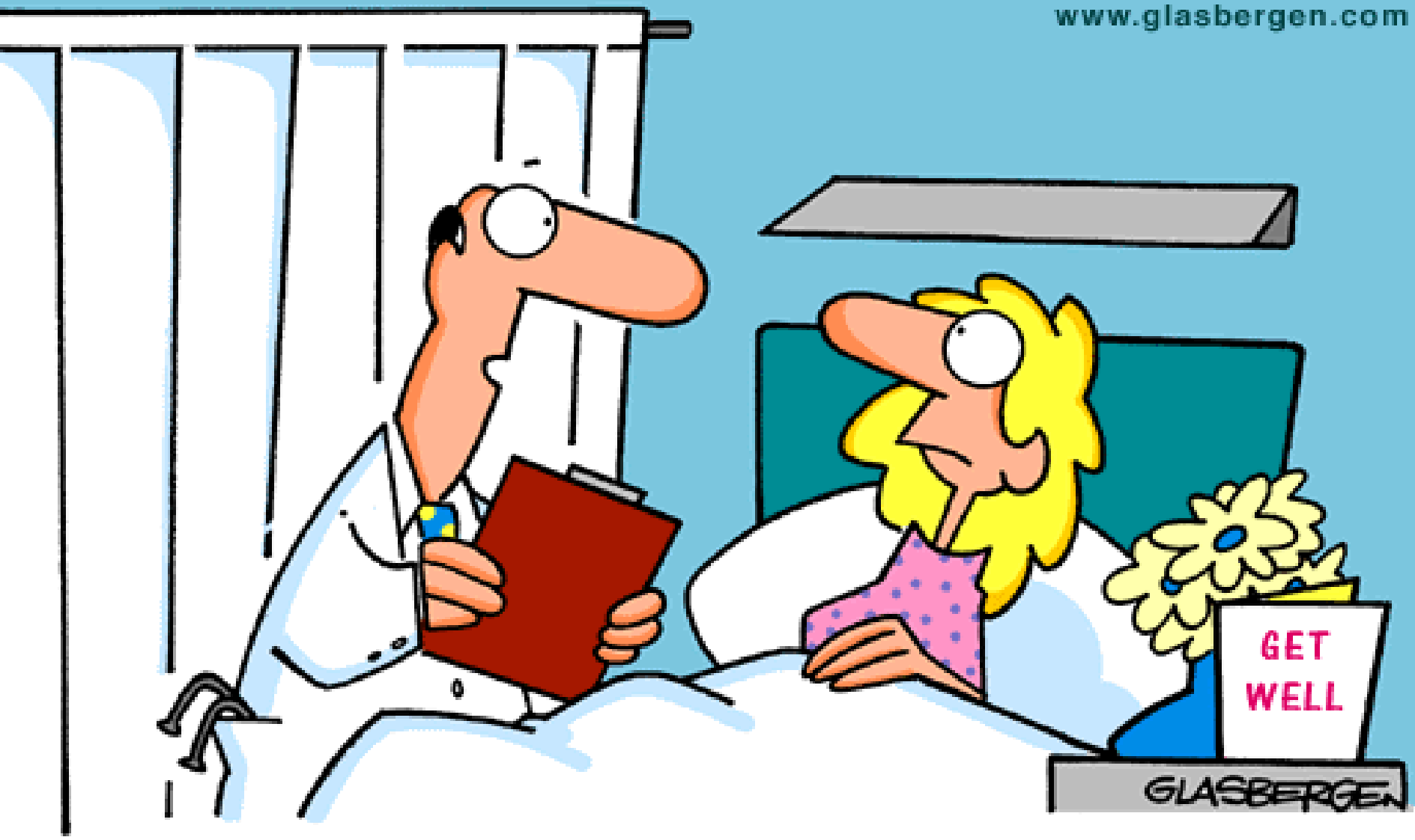
EXAMPLES OF FRAUD

- Tampering with eligibility criteria for inclusion/ continuation
- Pt. disguised & entered several times
- Pts. enrolled in other concurrent studies
- Investigator enrolling himself in study
- Forged Consent Forms
- Falsifying EC approval
- Fabricating lab results
- Charging for test article
- Plagiarizing Publications



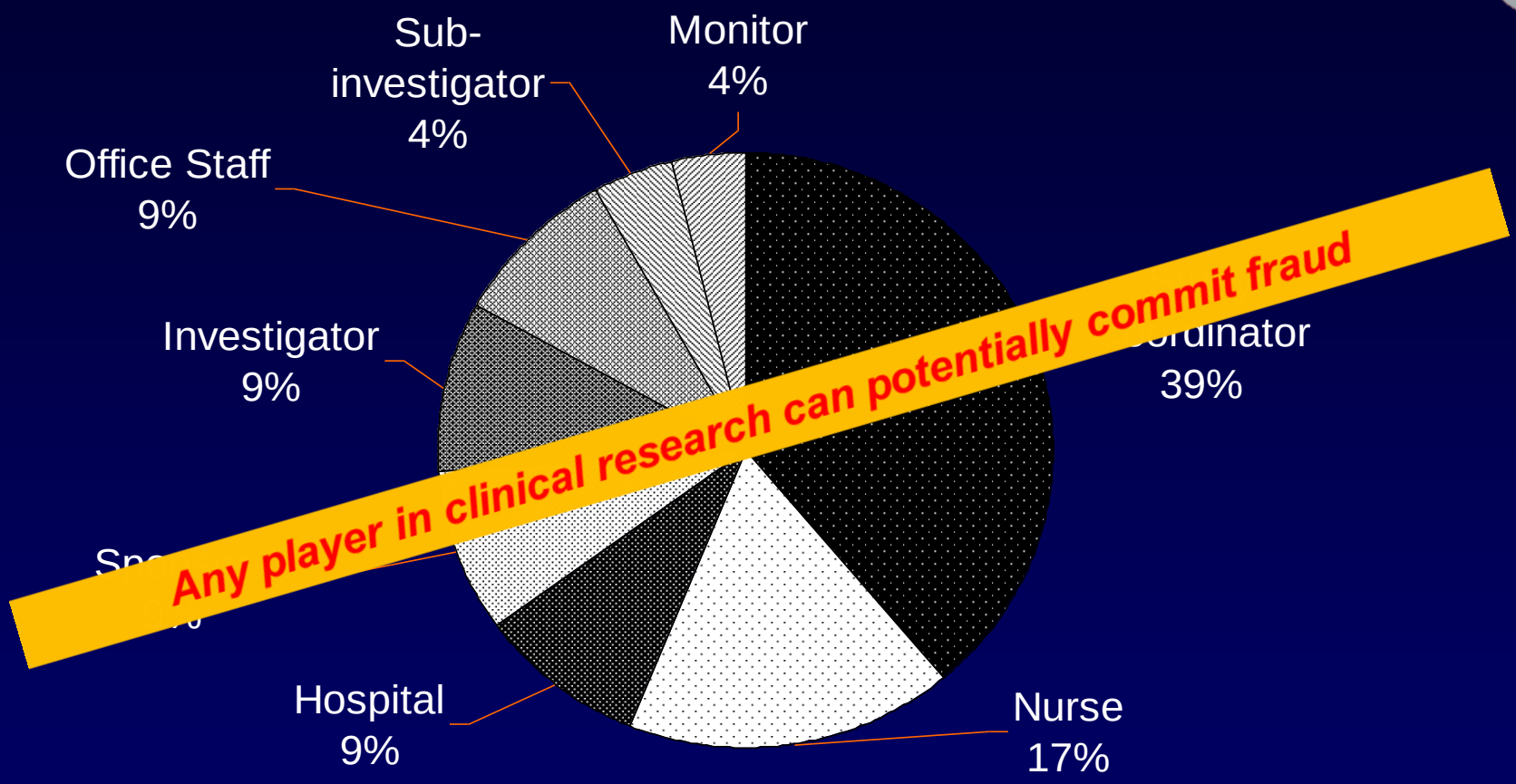
"As to the (forged) signatures of 4 out of 80 patients...we are talking of a margin of error of 5%- this is within recognized statistical limits."- Dr. Robert Fiddes

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"I dont think this is an SAE, after all you did not need that appendix, did you?"

THE BLAME GAME - WHO GETS THE BLAME ?



IMPACT OF FRAUD

- Patient abuse & exploitation
- Integrity of submitted/ published data – questionable
- Rejection of data/ reanalysis without suspect data
- Licenses issued based on unreliable data - Public health endangered
- Waste of public finances

MANAGEMENT STRATEGIES

Prevention

- Identify and eliminate/ minimize risk factors

Detection

- Monitor and recognize signs

Correction

- Promptly investigate and report findings



One should be able to Prevent, Recognize and Report

PREVENTIVE MODALITIES

Simplify workflow

Careful Selection of Investigators

Clear Communications

Minimize use of enrollment incentives

Train, share uncertainties

Equip teams with money, machines & men

Close Monitoring

Motivate workers

Strict Auditing



Interim Data Review

GATHERING PROOF

- Remain discreet – do not accuse !
- Look for:
  - Perfect documentation
  - Patterns across patients
  - Spurious data
  - Tampering of documents
  - Deviation from other centers
  - Suspicious behavior



"There is nothing like first-hand evidence"

DETECTION TOOLS

- Get Technical- Read ECGs, lab results, don't just inventory
- Fill in the Blanks - Question missing dates & time
- Don't be intimidated - tell the emperor he has no clothes
- Don't shoot the messenger - believe the monitor, put the burden of proof on the person suspected
- Beware of blame shifting
- Cultivate whistleblowers - establish rapport with study staff, be approachable and available, listen to grievances

"There is nothing more deceptive than an obvious fact"

THE ART OF DETECTION

"When you have eliminated all of which is impossible, then whatever remains, however improbable, must be the truth"



- Sherlock Holmes

WHEN FIRST DETECTED

- Do not suppress suspicions
- Handle discretely
- Do not reveal suspicions at site
- Do not immediately start using terms such as “fraud”
- Seek advice and help
- Confirm suspicions with objective evidence
- Collect circumstantial evidence and data

ACTION AGAINST MISCONDUCT

- Warning letter to investigator; demand improvement
- Increasing monitoring activity and training
- Act to save data at the site – where feasible
  - Correct the documentation
  - Reconsent all patients
  - Validate all data → modify the database
- Justify exclusion of data from final report
- Worst case : close centre and avoid using again

Principal steps on detecting misconduct: saving the data and ensuring patient safety

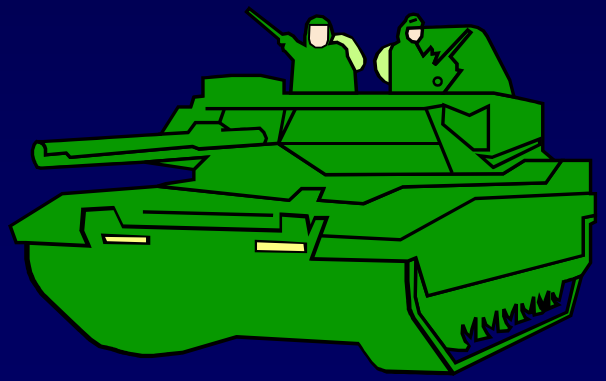
RESPONDING TO FRAUD

- Vital to have a company SOP to follow
- Initiated by suspicion by any member of staff
- Suspicion reported to line manager
- Suspicion relayed to operational manager and/or QA
- Evidence reviewed to substantiate or remove suspicion
- If substantiated, promptly notify senior management (& sponsor)
- Undertake for cause audit and statistical data review/ analysis
- If confirmed, determine course of action as per SOP

Data probably compromised beyond recovery

ACTION AGAINST FRAUD

- Close errant centre and prevent future use
- Inform the relevant regulatory agency
- Inform the errant investigator's institution/ professional body
- Inform the Ethics Committee



Understand that fraud cannot be fully eliminated and work towards minimizing it

SANCTIONS

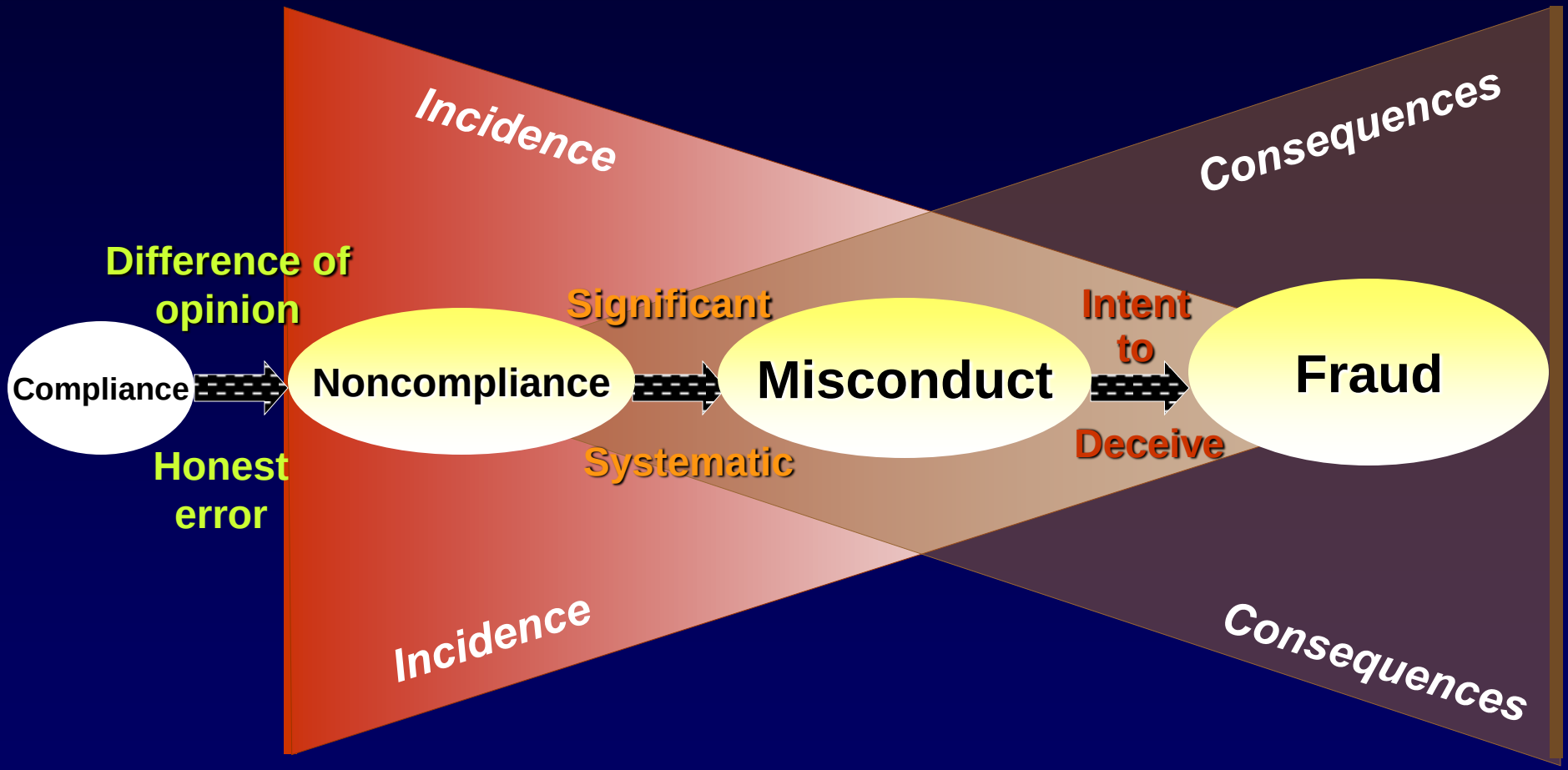
- Indemnification withdrawn
- Initiate disciplinary action
  - Professional
  - Institutional
  - EC
- Potential for civil or criminal prosecution
  - Breach of contract (e.g. Inv. Agreement)
  - Deception
  - Compensation (e.g. recover financial losses)



WHO BELLS THE CAT?

- UK
  - ABPI (medical director networking)
  - GMC statutory declaration
- USA
  - FDA maintain a list of restricted or debarred clinicians (www.fda.gov/oc/oha/list2)
- Nordic Countries
  - Denmark : Committee in Scientific Dishonesty (health & medical science)
  - Finland : National Research Ethics Council
  - Norway : National Committee for evaluation of Dishonesty in Health Res.
  - Sweden : Committee for Research Ethics, Expert Committee
- Germany
  - “Golden memory” of the Deutsche Gesellschaft fur Pharmazeutische Medizin

THE NON COMPLIANCE CONTINUUM



Anybody can commit it, Somebody should detect it, Everybody should minimize it

Most of Physicians

Inquiry for Study



Signing CTA



IM & Training



Site Initiation



Beginning of Recruitment



Ongoing Activities



Towards the End



NO MORE STUDY







THANK YOU

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