



Risk Based Approach (RBA) to Adjudication

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A key driver for Pharma Companies and the essence of the RBA

Adjudication \neq Quality

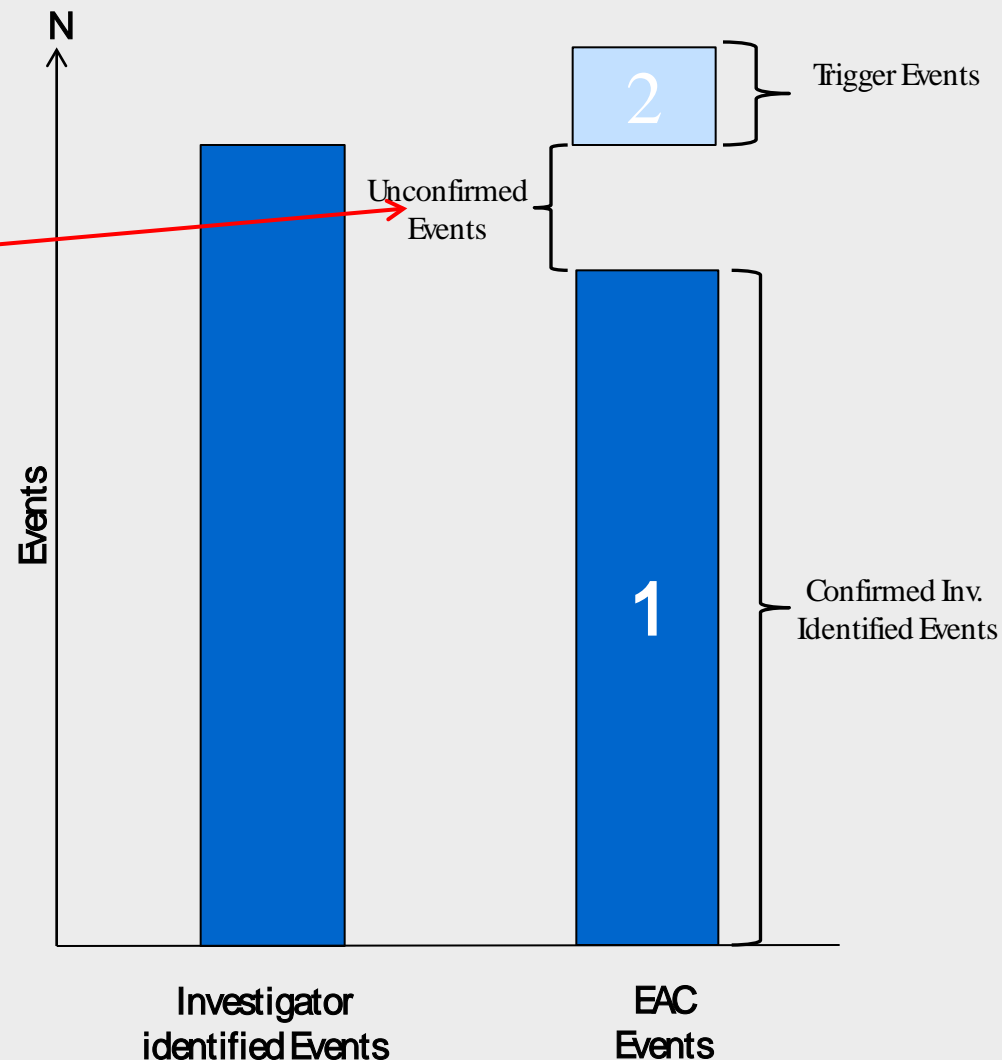
Adjudication implies Consistency = Quality

Quality means defining / measuring / assessing against a standard

1. Use an Adjudication vendor
 - standard process and contract e.g. Adj Charter before any work conducted and with protocol (whenever possible)
 - isolation from adjudicators
 - knowledge base
2. Inter-rater agreement between Investigators and Adjudication
3. Re-read process within adjudication process to determine quality, Inter-rater statistics (not required if (2) $>90\%$)

Investigator Identified / Adjudicated Events

- Confirmed events
 1. Adj. agree with Inv.
 2. Trigger events
- Unconfirmed events
 - Identified by Inv, not confirmed by Adj.
- Reasons for lack of agreement
 - Charter Definition \neq Protocol
 - Different specialist field e.g. CV vs CNS
 - *Unblinded Adj. (do not allow this)*
 - Different interpretation
 - Lack of evidence
 - Errors!



Adjudication of CV endpoints e.g. MI in large scale, global trial

Two methods to apply RBA, both variations on sampling

1. Base on supplied documentation / quality of documentation
2. Sample percentage from batches over time

1. Base on supplied documentation e.g. MI

Level of documentation is a key factor in confirmation of an event

- a. Case with ECG and Enzymes just take a sample to Adjudicate to demonstrate consistency (quality)
- b. Case with only ECG or Enzyme or neither then Adjudicate all

2. Set a target for an inter-rater agreement level

Sample percentage from batches over time.

Provided that samples are within the defined limits accept Inv. determination - Utilise QC techniques e.g. CUSUM.

If inter-rater agreement is below expectations, increase sample size or move to 100%.

Greater sophistication can come from assessing on a country or regional basis if there are differences

