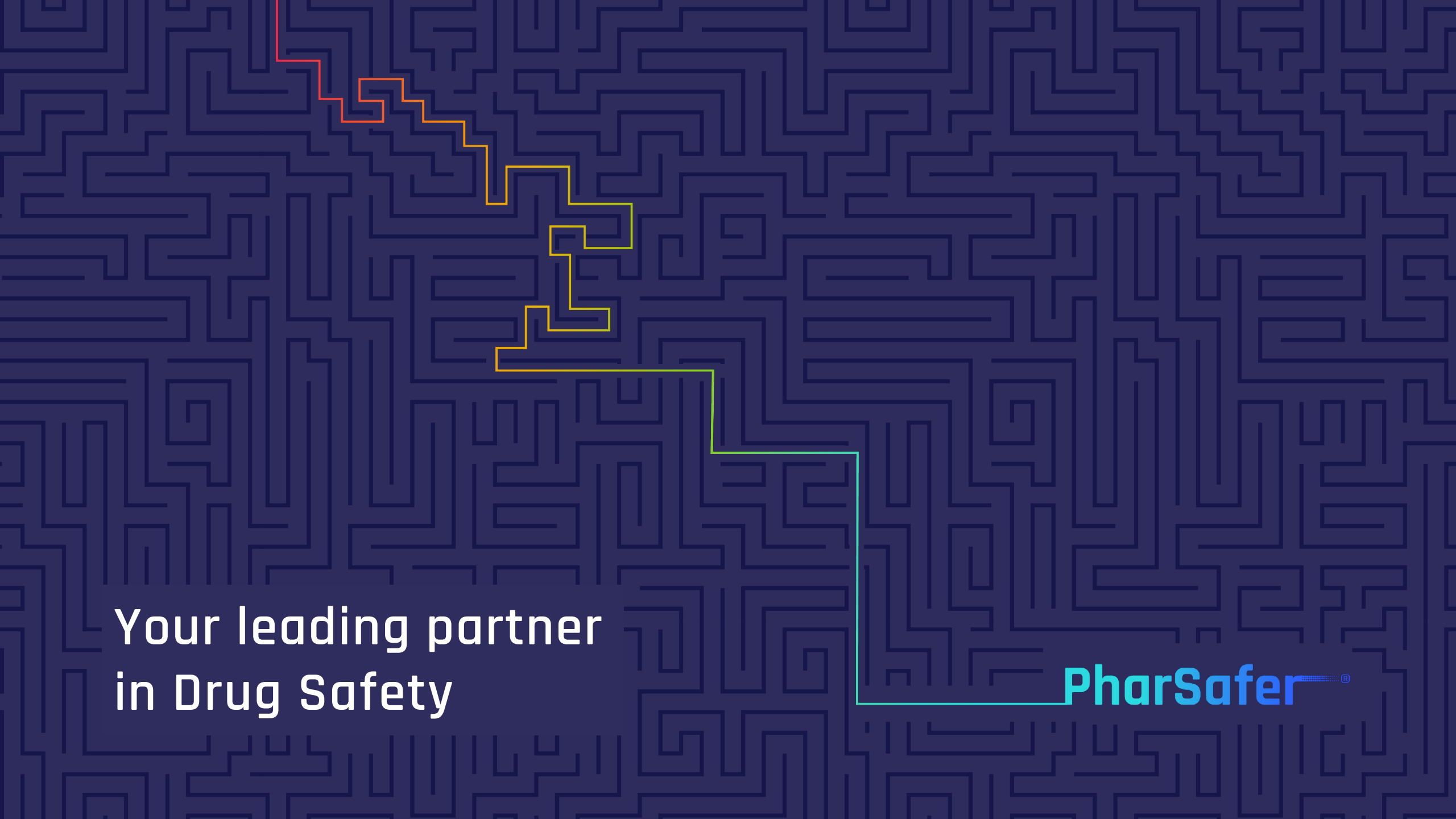
Your leading partner
in Drug Safety
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WHO ARE PHARSAFER?

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Founded in **2003** by **Dr Graeme Ladds**, PharSafer® is a specialist Global Contract Research Organisation (CRO) in **Global Clinical and Post Marketing Drug Safety, and Medical Services**, with a wealth of experience in Pharmacovigilance, Medical Affairs and Medical Information – and the various, numerous and extensive legal safety/medical obligations for licence holders to comply with.

Dr Graeme Ladds

- First degree in Biochemistry and Pharmacology and a PhD focusing on drug metabolism and Pharmacokinetics
- Over **30 years** experience working in areas of Drug Safety and Medical Services
- Former Head of Global Pharmacovigilance for a multi-national innovator Company and EU QP PV for several of the top ten Pharma Companies
- CEO and Owner of PharSafer® – a position held for the last **20 years**

Case Processing – The Most Important Part of Pharmacovigilance?

OR RUBBISH IN, RUBBISH OUT?

The conundrum in Clinical Drug Safety has always been:

Positives

- High quality safety data
- Data complete for causality assessment
- Ease for obtaining follow up information
- Trained reporters/Investigators
- Outcome/resolution data can be obtained
- Compliance to dosage intake monitored

Negatives

- Limited patient exposure
- Limited patient diversity
- Few SAEs/SUSARs to analyse
- Rare/Very rare events will not be seen
- Inclusion/exclusion criteria can prevent some serious ADRs being obtained
- Long term usage limited for possible long term side effects

The conundrum in Post Marketing

Positives

- Extensive patient exposure
- Large patient diversity – including off-label usage
- Lots of suspected ADRs (serious/non-serious) to analyse
- Rare/Very rare events will be seen because of extensive patient usage

Drug Safety has always been:

Negatives

- Poor quality safety data
- Data incomplete for causality assessment – difficult
- Difficulty for obtaining follow up information
- Untrained reporters (HCPs/Patients)
- Outcome/resolution data cannot always be obtained

Industry Challenges:

From Safety Data Intake to Signal Detection

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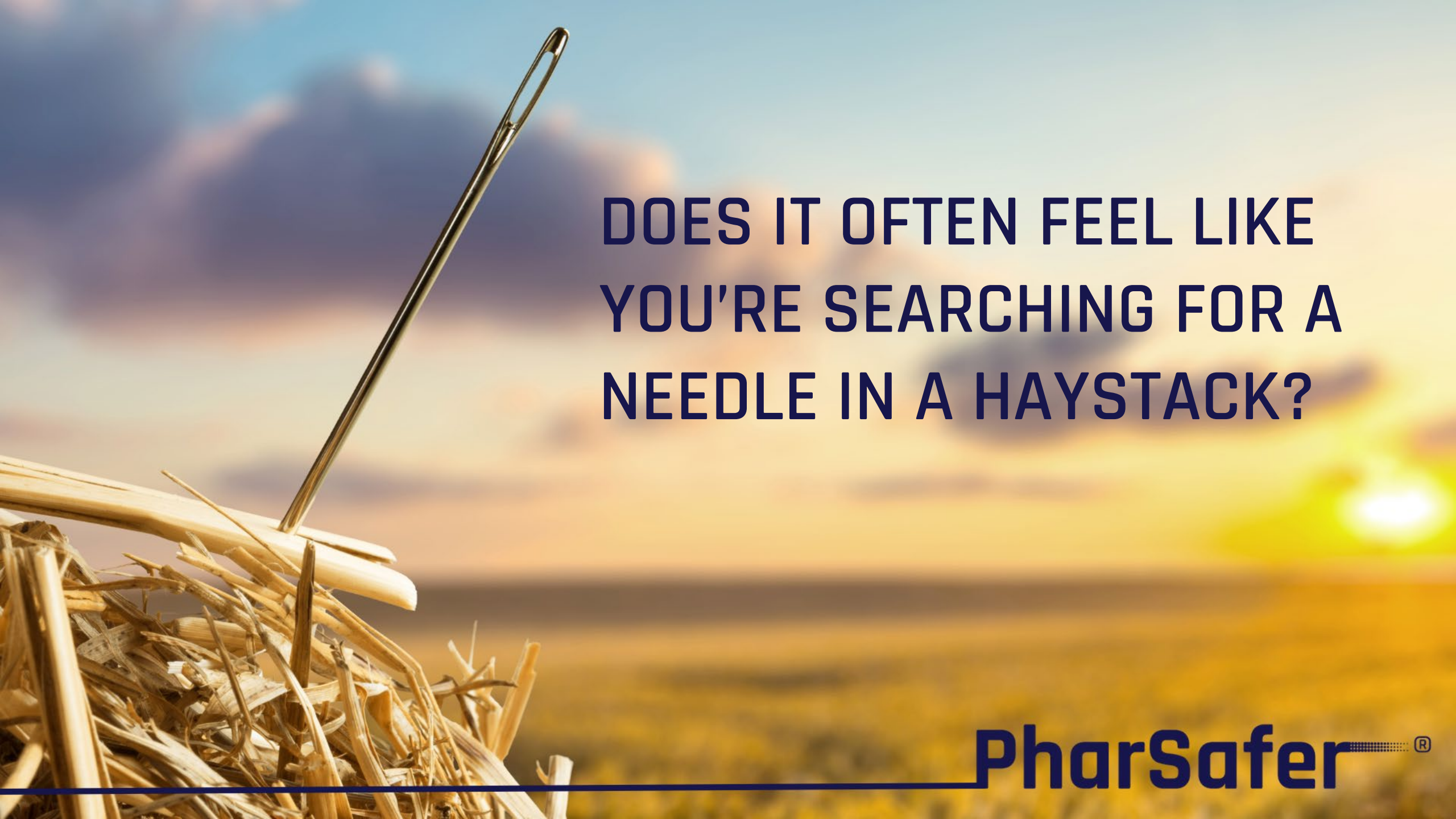
DOES IT OFTEN FEEL LIKE
YOU'RE SEARCHING FOR A
NEEDLE IN A HAYSTACK?
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This leaves us with the following situation:

Clinical Trials:

- An initial approved label that may be incomplete because of lack of safety data from patient exposure in clinical trials (ICH E1A; PDUFA III; ICH E2E);
- An incomplete Benefit-Risk profile as it is still evolving – Reg. Authority problem?
- Unresolved signals because of lack of data (ICH E2E; PDUFA III);
- Possible issues in more diverse patient groups (ICH E5; ICH E7; ICH E11)

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This leaves us with the following situation:

Post Marketing:

- Demand for case processing activities continues to rise;
- Post marketing case intake activities remain a very manual process;
- Significant amount of manual work required when reviewing literature search results;
- Ensuring follow-up requests are undertaken in a timely manner or even missed can often prove challenging for any Safety Department;
- Limited AI and automation tools on the market need to cover the wide range of product types – drugs; devices; vaccines; biologics etc..... For the different data fields

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From a practical perspective, this can mean the following happens when the product is marketed:

Reporters (HCPs; Patients)

Multiple reports – Serious and non-serious; expected & unexpected; invalid reports

Inaccurate data, incompleteness and reducing quality

Misleading analysis, poor periodic reports, inaccurate benefit-risk determinations due to flawed signalling

Serious regulatory findings!

Data Sources:

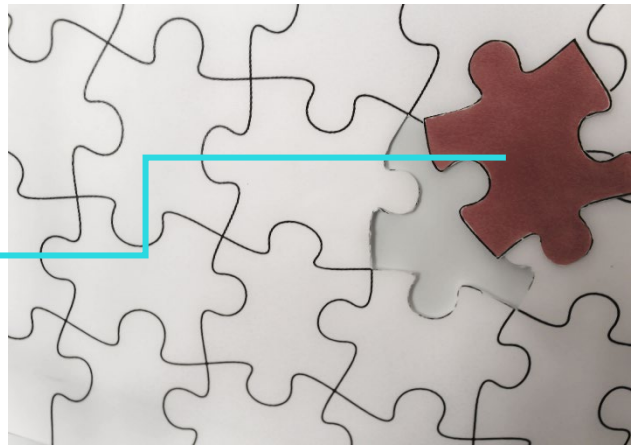
Direct reports; Scientific and Lay Literature; post-marketing studies; PSPs; Compassionate Use; Market Research Programmes; Investigator Initiated Studies; Partners - Distributors

Safety Data Intake issues

Pieces of the safety jigsaw that do not fit together:

Conflicting data; incomplete data; lack of follow up

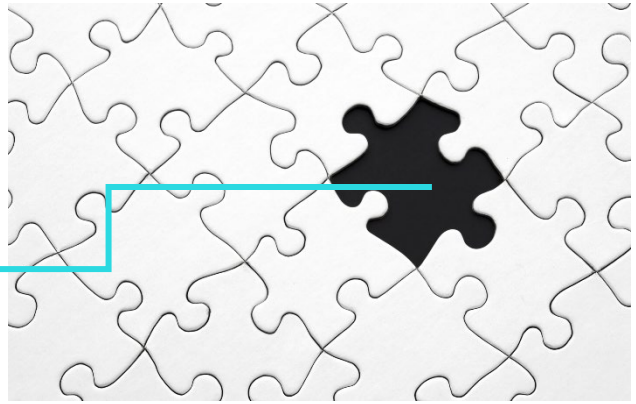
Signal Information doesn't fit



Pieces of the safety jigsaw that do fit together:

However, due to lack of data do not provide enough data for clear causality determination – the picture cannot be seen

Signal Information incomplete



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What else influences the speed of signal detection?

Company:

- **Staff training** – from case processing to signal analysis:
  - Consistency;
  - Continuous;
  - Developmental – (EU Module I)
- **Resourcing** – is it adequate in numbers **AND** experience?
- **Process** – do the Company processes enhance data quality/completeness?
- **Monitor** – does the Company monitor data accuracy/quality/completeness over time?

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What other factors are influencing safety data capture and processing?

- Since the **1960's** the number of **adverse reaction reports** received by pharmaceutical companies and Regulatory Authorities has **risen year after year**;
- **Emerging markets**, such as the cosmetics and medical devices industry, have **grown** exponentially, bringing **new and additional legislation** into the world of post marketing safety processing;
- Increasing **demand** for **case processing** & **analysis**; increased **cost of staffing** and **time processing**;
- Resulting in a significant, **ever-rising cost of training** for personnel, due to **continuous updates in legislation**, increasing **demands on compliance and accuracy** which increases the possibility of **processing errors**;

Finally – COVID – Business continuity (EU GVP Module I) – causing delays; errors and lack of follow up

What other factors are influencing safety data capture and processing?

- If the initial reports received are **containing little information**, this means that **understanding what has happened** to the patient and why can be **very difficult** without obtaining **follow-up information**;
- Most spontaneous post-marketing reporting systems for the reporters (excluding Company personnel) are **voluntary** – as is the provision of follow-up – which means that **multiple attempts** may be made by the Company to obtain the **essential additional information** to **determine causality**;
- This also assumes that the case processing team have been **trained** to understand what to ask for by way of follow-up with **targeted information requests** – as opposed to sending out **'blind'** ADR forms requesting completion;
- The assumption as well is that the **reporter** knows what information we **require** for our **assessment**?

Current Industry Structure

So, what is the solution?

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Is this really the solution to your case processing problems?
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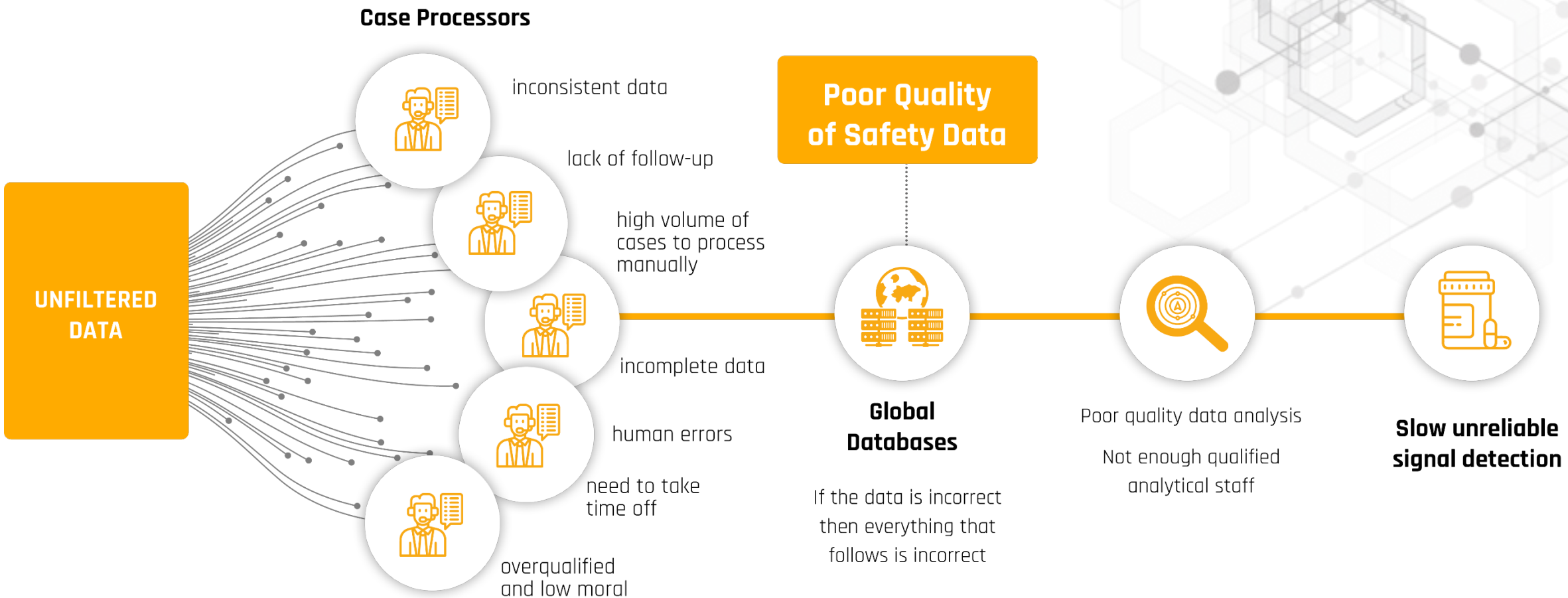
Process without automation



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Reshaping the Industry

Case processing staff are top heavy, expensive and management is intensive for training

We want a bottom heavy environment for greater amount of time reviewing and determining signals from accurate and complete case reports

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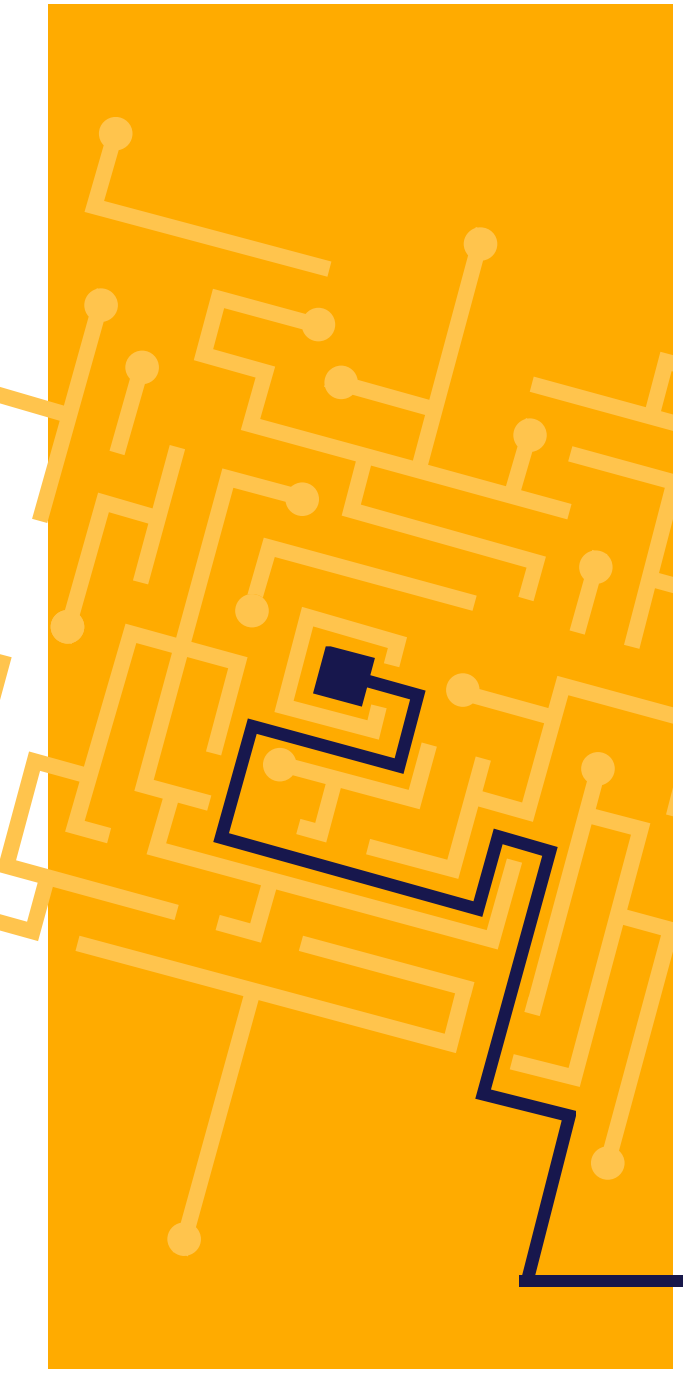

The solution?

Not a single solution but multiple ones:

Automating case intake:

- The suspected adverse reaction journey from reporter to Company;
- Allowing the reporter to know what we wanted in the report – as opposed to them guessing – **important** and **required** data field completion;
- Simplifying the ADR form for patients versus Healthcare Professionals

Intelligent case intake – **Nonsense** data checks:

- The system identifies reporter errors for them to correct real time BEFORE reaching the Company

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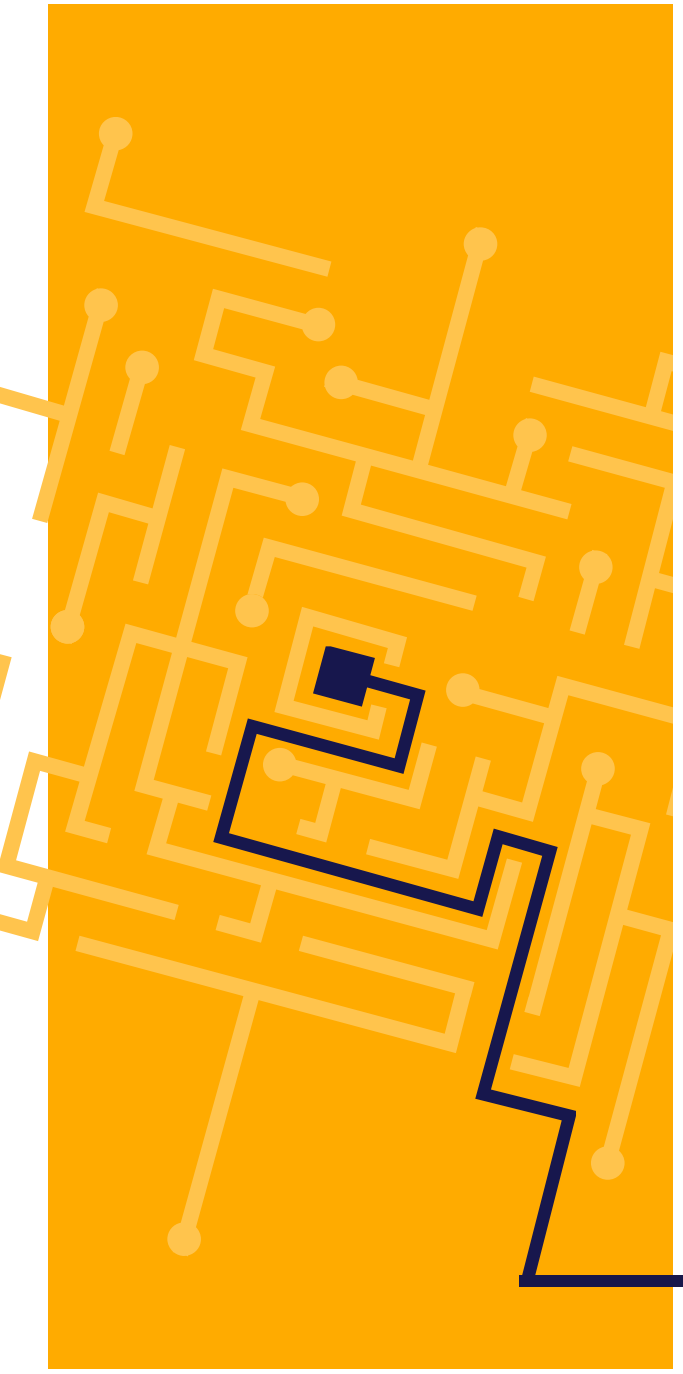

The solution?

Not a single solution but multiple ones:

Automating case intake:

- Provides **simple** completion through drop down fields for completion;
- Is **multi-lingual**;
- Allows **delivery into any safety database**;
- Provides safety data in a **consistent** and **standardised format**;
- Performs **configurable** and **flexible case follow up**, timed and focussed AND sensible

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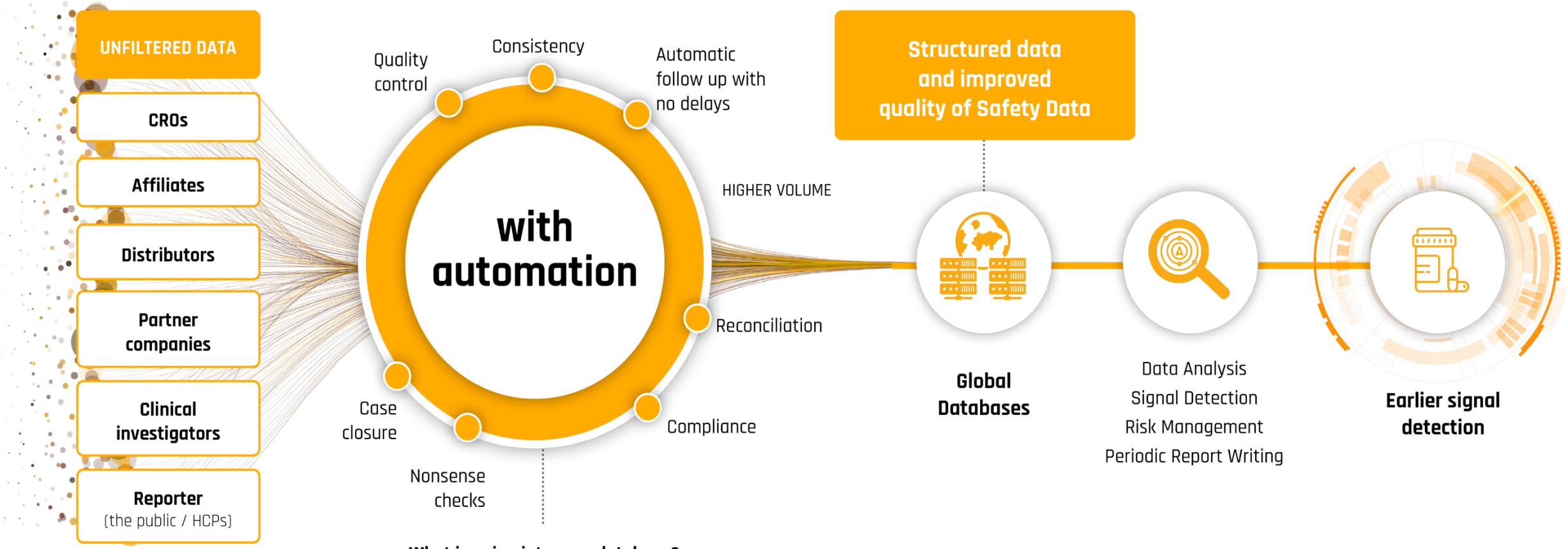
The process with automation



What is going into your database?
How complete are your cases?
RAPTAR can answer regulatory authorities questions on quality
MHRA can fine you and your products removed from market
You don't want to be penalised if not done properly

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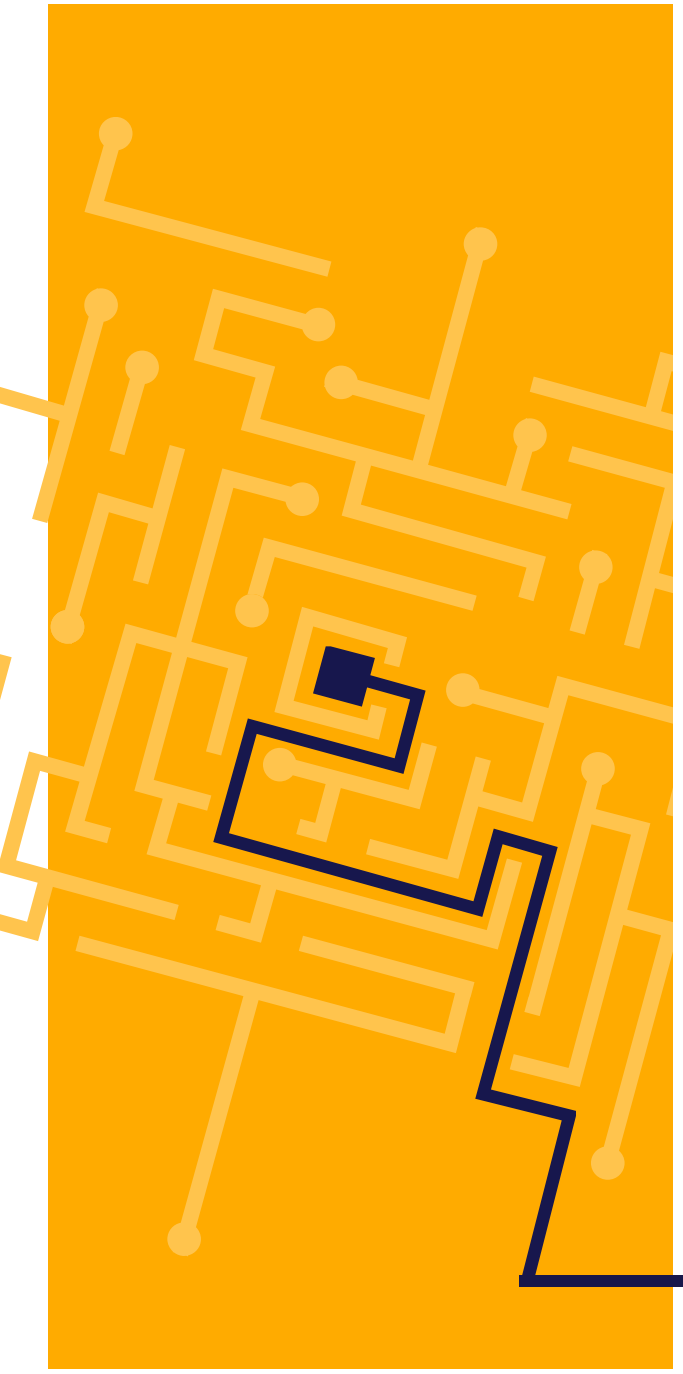

So, what is left for QA?

Still much to do:

Any automated system must demonstrate major defined advantages over existing manual processes.

This requires:

- Review of **case processing time** – is it quicker/better;
- How many cases **will not** automatically import into the database; needs to be 80% +?
- Has the **quality** of the cases improved – less errors/conflict data;
- Is more **follow-up information** being received than manually?
- Are the cases **more complete** allowing **easier determination** of causality?
- Analytics of any Automation process

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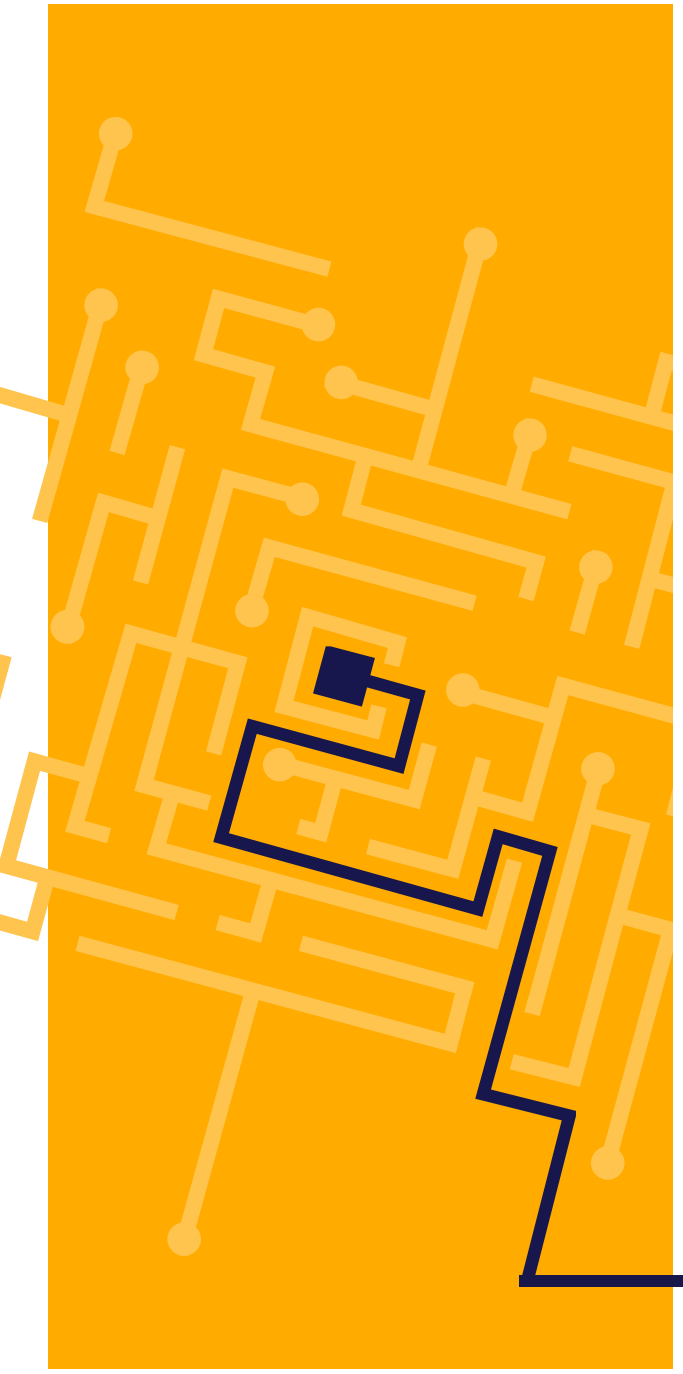

Ultimately…

The automation has to show:

- **Consistency of information** globally – monitoring reports by country;
- **Reproducibility** for the various types of **reports**; drugs; devices; vaccines etc…
- **Reproducibility** for the types of **cases** for the varied Company product types – cardiovascular; gastrointestinal; oncology;
- **Speed** – has to show much greater efficiency in data capture (for reporters) and processing
- **Cost** – Have we created a better more cost efficient system because it operates 24/7, schedules and chases follow up;

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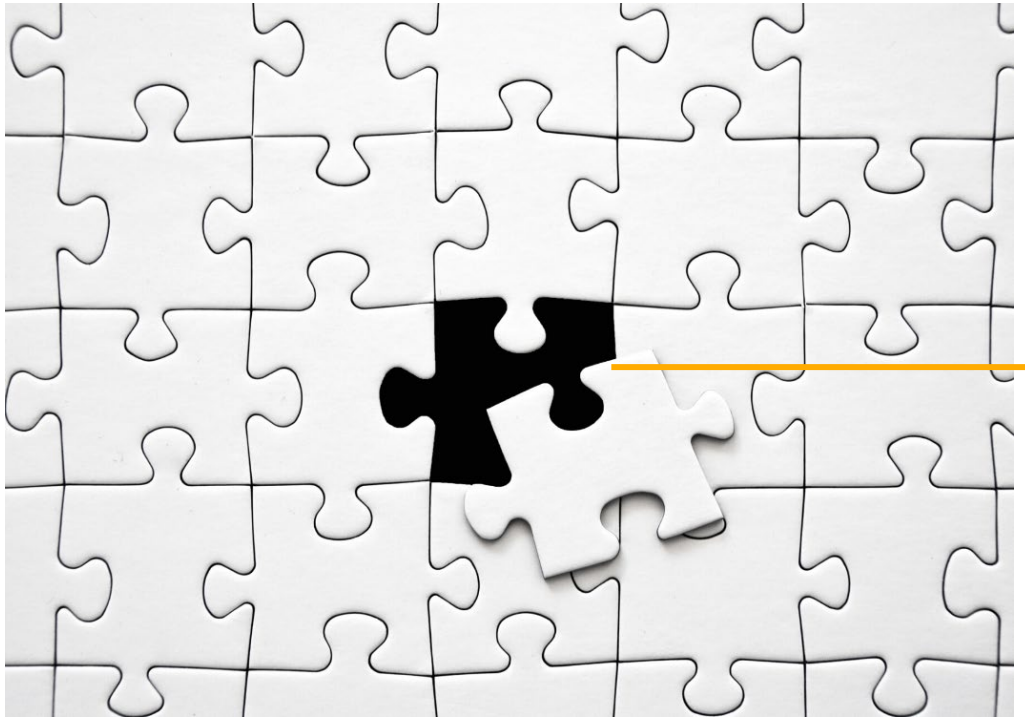
And finally…

Can signals be identified earlier, with fewer cases required to highlight potential problems as a result of better reports which allow easier causality determination?



Signal Information more complete


BOOTH 105
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TRANSFORM IT WITH R.A.P.T.A.R®
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Guiding you to BOOTH 105 and a clearer, (Phar) safer future

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