

DEVELOPING YOUR CONTENT

Study the scientific results

The Trial Results



Research Report

- Inspect
- Examine
- Scrutinize

A clinical trial yields a wealth of research results. There are usually primary and secondary parameters. Do your homework and inspect the scientific results thoroughly. Review them carefully. You may have to dig deeply. Enlist the support of colleagues from the clinical development or the medical marketing department, or of an outside consultant, to help you.

Interpret the data

The Meaning of the Results

Interpret the constellation of data and give them meaning



Make sense of the results

Give meaning to the results by answering the following questions:

- what does the data mean to the doctor?
- how do you interpret the results so that they are relevant to the doctor?
- which conclusions can you draw for the practice of medicine?

This task takes a razor-sharp mind, time and commitment. Do *not* expect your advertising agency to do this for you – they usually lack both the medical expertise and the research background.

Develop your message

From Results to Message

Results: The set of numbers, tables, diagrams and charts

Give meaning

The Message:
What you want to convey to your customers

Based on the trial results and the meaning you attribute to the scientific findings, develop answers for the following questions:

- what is your core message?
- what do you want to communicate?
- what is your story?

Take the time to think.

Ensure that your message is based on scientific evidence.

Positive Result: Message



Scientific result

HIV test is positive ...



Patient message

You've got the HIV virus

An HIV (human immunodeficiency virus) test usually shows either a positive or a negative test result. A *positive* test result is bad news for the patient (who has been infected with a deadly virus). A positive result implies the following message to the patient: 'You are infected with HIV'.

Negative Result: Message



Scientific result

HIV test is negative ...

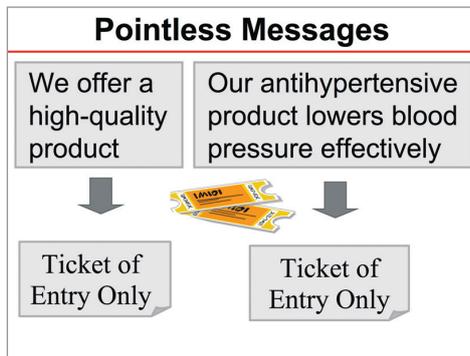


Patient message

Everything is fine

A *negative* HIV test result usually means that the patient has not developed antibodies against the human immunodeficiency virus: positive and encouraging news for the patient. The underlying message is: 'Everything is fine'. However, a poorly developed and communicated message can have devastating consequences. In the past, patients told that 'Your HIV test is negative' have misinterpreted the statement as meaning 'You have the disease'.

Avoid irrelevant messages

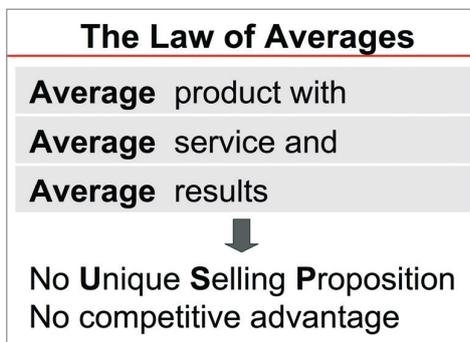


One company for which I undertook consultancy work considered promoting their new product as a 'high-quality' product. However, most products on the market were considered 'high-quality' products. Hence this is a marketing approach that does not communicate any competitive advantage. We therefore changed the message.

A second company marketed their new blood-pressure-lowering drug as 'effectively reducing blood pressure'. Yet this is exactly what you

would expect of all blood-pressure-lowering drugs. Once again, this approach does not communicate any competitive advantage.

Look for competitive advantages



The market is flooded with competing products using similar messages. Are the characteristics of your product, your service and your trial results different from those of your competitors? Does your message convey a competitive advantage?

Work the angles considering all data

Unique Selling Point

Ask: How is the trial unique?

In what way is the trial special?

What distinguishes the trial from all other trials?

How are the results distinctive?

Look for an angle that lends support to a unique or special claim for your drug. You need to stand out from the crowd. This is not about being experimental or extravagant in your claims, just about being distinct. Ask yourself: how is your trial special or unique in design or results? How are the results relevant to better patient care?

Always communicate a balanced risk-benefit ratio.

Ask the right questions

The Right Question



Example significantly prolongs ...

Survival ?

Event-free survival ?

Cardiovascular event-free survival ?

Cardiovascular event and procedure-free survival ?

There are often nuggets of information you can extract from the wealth of research results. Information needs to be both clinically relevant and helpful in distinguishing your product by supporting a competitive advantage. Sometimes asking yourself the right questions can help identify the appropriate answer in the research data. Probe in different directions. The example shows how you can fine-tune your questions.

Seek insights from the investigators

The Investigators



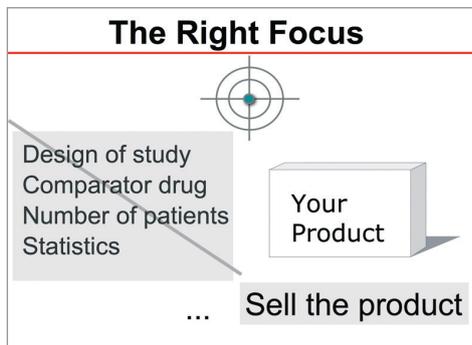
An immense knowledge base

Discuss questions with clinical investigators

Gain insights from the experts

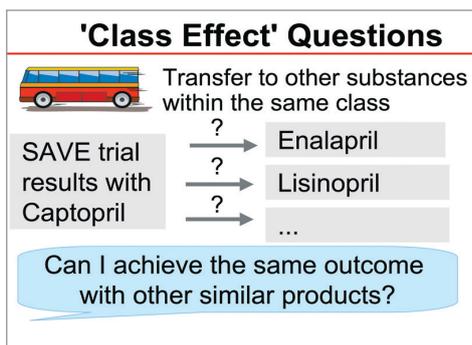
The clinical researchers who undertook the trial form a huge knowledge base. Talk to them. Ask your medical colleague to introduce you. You will usually be given a warm welcome. Make time for a chat with them. What were their experiences of the trial? What impressions and ideas can they offer?

Set the right focus



You need to emphasize the benefits of the product and not the characteristics of the trial. Details about the number of patients, design of the trial, statistical considerations, comparator drugs and so on should be kept firmly in the background. Highlight what the product can do for the doctor and the patient. Always remember: ‘Sell the product, not the trial’.

Beware of questions about the ‘Class Effect’



The ‘class effect’ refers to the potential interchangeability of substances within the same chemical class. Experts like to raise this sensitive issue during symposia and workshops: ‘Can the study results be transferred to other substances within the same class?’ or ‘Can I achieve the same outcome with other similar products?’

One example involved a discussion about the clinical equivalence of ACE inhibitors (a class of antihypertensive drugs). The SAVE (Survival and Ventricular Enlargement) trial done with the

ACE inhibitor Captopril showed results in favour of that substance. Captopril reduced the risk of mortality attributed to cardiovascular events by 21 percent.

Keep tight-lipped about theories

Question Handling	
The Others	Your Product
 <p>Enter into discussions</p>	<p>We have got the data. They don't.</p>

The company sponsoring the SAVE trial and subsequently marketing Captopril was Bristol-Myers-Squibb. When a representative was asked the 'class effect' question, his answer was along the following lines: 'We have the data, they don't' (with 'they' implying the competitors). Use similar statements if you are asked similar questions and leave it at that. This is one of the rare occasions when you should be absolutely tight-lipped. Resist the temptation to speculate. You have the scientific evidence and the other companies do not.

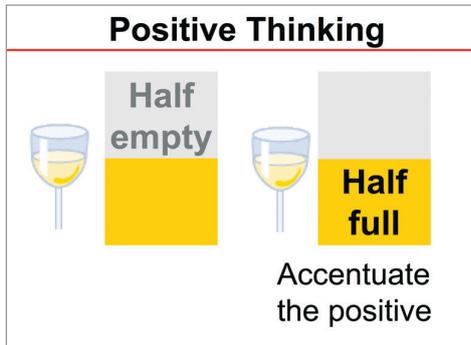
Learn the power of language

The Other Treatments	
control	} Avoid in core message
standard treatment	
conventional treatment	
another widely-used substance	
reference substance	
Conventional treatment (INSIGHT)	
Another widely-used substance (COMET)	

In your discussions, you may need to talk about alternative forms of therapy. How should you refer to them? When discussing the INSIGHT trial, Bayer used the term 'conventional treatment' or 'standard treatment' to describe the diuretic treatment arm. When justified by the results, these terms establish the expectation of a treatment improvement. In the COMET, Carvedilol or Metoprolol European Trial, metoprolol was referred to as 'another widely used substance', essentially a neutral

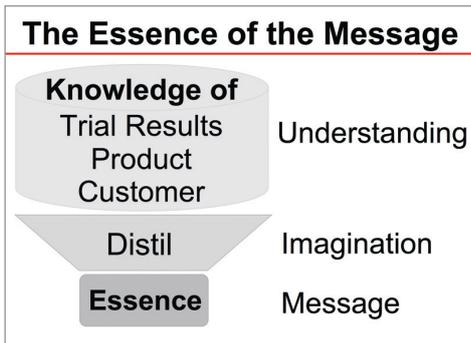
description. You should avoid the term 'reference substance' because this implies the definitive treatment. Your final message should always highlight your product and not the other form of treatment.

Think positive



Successful marketers have a mindset that focuses on the positive. This is a useful approach for marketing clinical trials. Marketers don't consider the glass half empty; for them it is half full. They don't ignore negative aspects, but they are able to highlight the positive and desirable ones. Keeping the right balance between the two and appropriately representing the risk-benefit-ratio of a drug is an art that can be learned.

Capture the spirit



You need to distil your detailed knowledge:

- of the trial results
- of the product characteristics, and
- of the customers' needs

into its essence. This task requires understanding and imagination. A clear and original message is crucial if you are going to communicate your competitive advantage successfully to your customers.

Create a convincing message

A Convincing Message

Concise	Short and to the point
Clear	Easily understandable
Credible	Endorsed by reliable sources
Consistent	Repeated in a uniform way

What makes a message convincing and compelling?

- Make it concise = short and to the point
- Make it clear = easily understandable
- Make it credible = in line with other information and endorsed by a reliable source
- Make it consistent = repeat the same message to all the people you communicate with (uniformity across people and time).

Keep it simple

A Clear Message



~~Everything is important~~

Keep things brief and clear

Keep it **s**hort and **s**imple

I know that details matter. As a medical director, I was responsible for ensuring that every detail of an advertisement adhered to regulatory requirements. However as marketer, I have learned to keep things short and simple: brief is better than long. You need to boil down and condense complex issues into clear, concise and crisp claims that everybody can understand. Keep the details for the specialists. There is no need to say everything. If in doubt, compress, reduce, shorten, abridge and summarize.

Major Results of XYZ Trial

The clinical study of A versus B resulted in risk reductions of

Primary endpoint

- 8% in all-cause mortality (non-significant trend: $p=0.128$)

Secondary endpoints

- 12% in combined all-cause mortality and all-cause hospitalization ($p=0.002$)
- 10% in cardiovascular mortality (non-significant trend: $p=0.073$)
- 8% in combined all-cause mortality and cardiovascular hospitalization ($p=0.036$)
- 9% in combined cardiovascular mortality and hospitalization ($p=0.027$)
- 8% in fatal and non-fatal ... and hospitalization ... ($p=0.374$)

Post-hoc analysis

- 15% in combined all-cause mortality and hospitalisation ... ($p<0.001$)

This piece is based on a real example. The original trial name has been changed to 'XYZ Trial'. The readers cannot see the message when confronted with all this complex information, nor will they bother.

Check for clarity

A Clear Draft



Ask: Is your draft

Easy to read?

Easy to understand?

Easy to remember?

Once you have developed a draft, please check:

- is it easy to read?
- is it easy to understand?
- is it easy to remember?

If you do not get a green light on all three items, change and simplify your draft.

Avoid pitfalls when developing content

The Main Pitfall



Saying more than is necessary and trying to put all the information into one single document

The most common mistake is to put too much information into one piece or document — whether it is an advertisement in a journal, a detail-aid folder for the sales force or a brochure for physicians. It is tempting for someone with a strong orientation toward research to try and cram too much information into a single document. These overloaded documents drown your message and your prospect will not even bother to read them.

Be concise

A Straightforward Message

Delete unnecessary items

Drop details that do not convey your message

Eliminate words that do not sell

Principle in Direct Response Marketing

Keep everything you do straightforward. Avoid superfluous words, styles, symbols and images. Pull out all the stops in your language while making sure that you represent the right risk-benefit ratio of your drug. Do not communicate more than is necessary: too many cooks spoil the broth and too many details confuse your message. Eliminate any details that do not help you convey your message:

- use simple language
- cut any words that do not sell
- satisfy the need for a quick read.

Move from Features to Benefits

From Features to Benefits

Mention

Offer

Features and Attributes

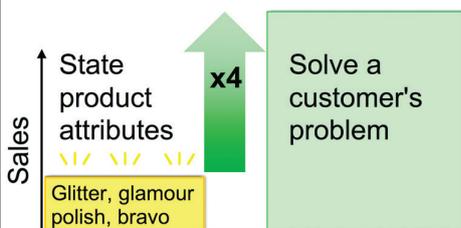
Relevance to the customer

Benefit

The customers are not interested in those features of your product or trial that have no relevance to their life (for example, details of statistical analysis). They are only interested in the potential benefits that you and your company can provide. Leaving human appreciation and financial rewards aside, your main benefit consists in solving a health problem.

Solve customers' problems

A Customer's Problem



Dr. Gallup, USA: Effect of content of TV spots on sales

Dr Gallup investigated the effect of the content of televised commercials in the US on subsequent sales for certain consumer goods. He found that – compared to stating product attributes (“the glitter and the glamour”) – commercials that purported to solve a customer’s problem resulted in sales that were four times higher. The conclusion: solve a problem and increase revenue.

Offer solutions

Providing Solutions?



Nice products
and nice trial
results ...



... will not
necessarily
solve problems

Why should your customers care? Are you helping them solve a problem? Are you helping them to find an answer to a question in their professional lives? Do you meet an unmet need? Is there a fit between what your customer needs and what you offer?

A new pharmacological breakthrough or the amount of substance used per tablet do not qualify as elements of a solution. Case in point: one pharmaceutical company built their message around the small dosage the patients had needed to take. They had prominently

displayed the term 'microdose' in their advertisement campaigns for a cardiovascular drug. They realized later that this feature does not lend itself to a convincing argument for the prescribing physician. They ultimately changed the slogan.

Follow the solution imperative

The Big Question



Product and
trial results



Which problem
do they solve?

Your offer must match the need

The following questions sound straightforward, but are essential to your success:

- which specific problems do you solve with your product and your trial results?
- are you sure that it is a problem or an unmet need for the doctor?

If your customers are not aware of a problem, they will not listen to you.

Work on these questions, until you have found a satisfactory answer.

You may need to sharpen doctors' awareness for particular problems. For example, companies marketing lipid-lowering drugs (especially statins) have successfully increased physicians' awareness of the risks of hyperlipidemia and the healthcare benefits of treating this condition resulting in tremendous product revenues.

Understand the real needs

The Doctor's Real Needs

My goals  The doctor is interested

- Improving patients' health
- Making patients happy
- Giving state-of-the-art treatment
- Saving precious time
- Being financially successful

Focus on the key areas in which doctors seek better solutions. Ensure that you provide the doctors you are targeting with solutions to the problems that concern them. Give them only the support they are really interested in.

Pin down your solution

The Dimensions of Your Offer

 Your product

Improvements in

- Efficacy
- Tolerability
- Convenience
- Affordability

Where do you provide a solution?

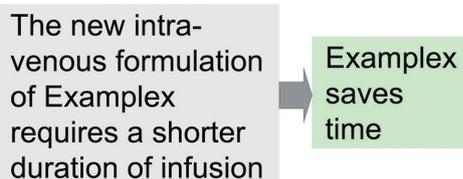
For most diseases, there are four areas in which your product can provide a solution. It may offer improved:

- efficacy (desired pharmacological effect)
- tolerability (the profile of side effects)
- convenience (user-friendliness)
- affordability (price).

You need to identify which of these elements is true of your drug.

Communicate explicit benefits

An Explicit Benefit I



The illustration shows how a shorter duration of infusion for a new drug results in a clear advantage for the patient and the healthcare professional. He or she saves precious time. This may seem obvious to you, but spell it out. Do not leave it to the physician to work out how features translate into benefits. Specify the benefit clearly.

An Explicit Benefit II



See also Marketing campaign for Cialis®
Treatment of erectile dysfunction. Cialis® is trademark from Lilly

This example shows how the pharmacokinetic feature of a longer duration of action and a longer half-life translate into a clear benefit. The concept 'more time for the right moment' is successfully used by the company Lilly for their product Cialis® in the treatment of erectile dysfunction.

An Explicit Benefit III



The once-daily administration of a medication results in better convenience and adherence to treatment (patient compliance) compared to a twice-daily medication.

Practical examples – The COMET Case Study

COMET: Scientific Data

Carvedilol in Heart Failure

In the Carvedilol or Metoprolol European Trial (COMET), around 3000 people with chronic heart failure were assigned to receive twice-daily doses of carvedilol or metoprolol for around five years. Yearly mortality rates were 8.3% with carvedilol and 10.0% with metoprolol. Average life-expectancy was eight years for patients given carvedilol compared with 6.6 years for patients assigned metoprolol. 34% of patients assigned carvedilol died during the five-year study compared with 40% of patients assigned metoprolol.

Based on presentations and The Lancet, 5 July 2003

The **Carvedilol or Metoprolol European Trial (COMET)** included around 3000 people with chronic heart failure.

COMET: Message to Experts

Carvedilol in Heart Failure

Results of a European study in this week's issue of *The Lancet* suggest that the beta-blocker carvedilol offers substantial survival benefit compared with another widely-used beta blocker for the treatment of chronic heart failure.

Based on presentations and The Lancet, 5 July 2003

Based on these results, the company conveys a clear message targeted at experts and opinion leaders.

COMET: Message to Physicians

Carvedilol in Heart Failure

Dilatrend® patients live longer, on the average 1.4 years*

*** COMET: Carvedilol versus Metoprololtartrat. The Lancet 2003;362:7-13**

Dilatrend® is a trademark from Roche
Based on translation from German "Deutsches Ärzteblatt", 12 September 2003

A clear message targeted at prescribing physicians.

The ACTION Case Study

ACTION: Scientific Data

Long-Acting Nifedipine in Angina

A Coronary Disease Trial Investigating Outcome with Nifedipine GITS (ACTION): Patients with treated stable symptomatic coronary disease: 3825 patients assigned to nifedipine and 3840 assigned to placebo

Findings: 310 patients allocated nifedipine died compared with 291 people allocated placebo (p=0.41). Primary endpoint rates per 100 patient-years were 4.6 for nifedipine versus 4.75 for placebo. With nifedipine, rate of death and any cardiovascular event or procedure was 9.32 per 100 patient-years versus 10.50 for placebo (p=0.0012)

Based on presentations and The Lancet published online August 31, 2004

A Coronary Disease Trial Investigating Outcome with Nifedipine GITS (ACTION) investigated the effect of long-acting nifedipine in patients with coronary artery disease.

ACTION: Message to Experts

Long-Acting Nifedipine in Angina

Addition of nifedipine GITS to conventional treatment of angina pectoris has no effect on major cardiovascular event-free survival. Nifedipine GITS reduces the need for coronary angiography and interventions.

Based on presentations and The Lancet published online August 31, 2004

Based on these results, the company conveys a clear message targeted at experts and opinion leaders.

ACTION: Message to Physicians

Long-Acting Nifedipine in Angina

A unique study due to its design, size and scientific validity

Proven safety and improved outcomes on top of best practice treatment: 11% additional risk reduction*

*Primary endpoint and interventions

Based on presentations and The Lancet published online August 31, 2004

A clear message targeted at prescribing physicians

The 4'S' Case Study

4 'S': Scientific Data

Scandinavian Simvastatin Survival Study

Although noncardiac death rates were similar among the groups, the relative risk of mortality (from any cause) was decreased 30%, and the relative risk of coronary mortality was decreased 42% in the simvastatin arm.

Based on presentations and the article by Pedersen TR: Coronary artery disease: the Scandinavian Simvastatin Survival Study experience. Am J Cardiol. 1998 Nov 26;82(10B):53T-56T

The **Scandinavian Simvastatin Survival Study** investigated the effect of simvastatin in patients with hyperlipidemia.

4 'S': Message to Physicians

Scandinavian Simvastatin Survival Study

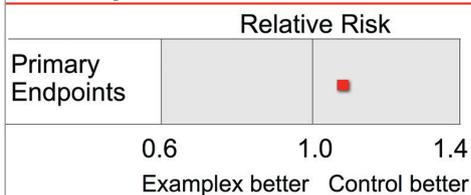
Zocor® Power for survival

Zocor® is a trademark from Merck & Co

Based on these results, the company conveys a clear message targeted at prescribing physicians.

The Exampex case study

Example: Outcome I

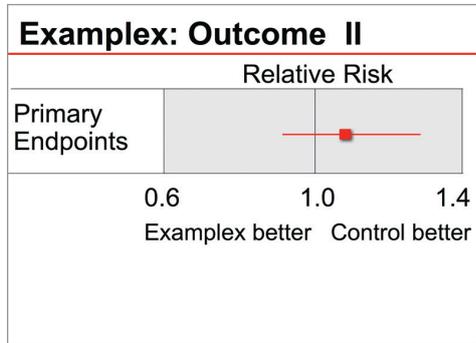


Which questions will you ask?

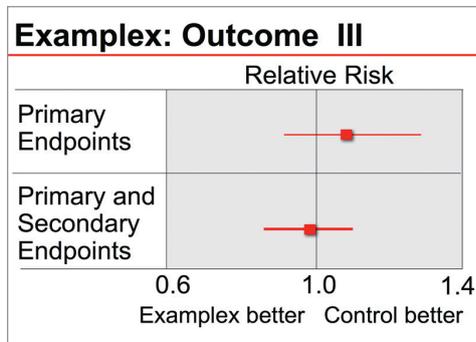
Our example company spent millions on a large international high-quality trial involving several thousand patients with a cardiovascular disease. We will call it the Exampex trial. The data were analysed.

You are the product manager responsible for product 'Exampex'. What set of questions will you ask? Subsequent illustrations show you how to use these questions to move through various drafts and arrive at a final version that provides a far more balanced view of the study results.

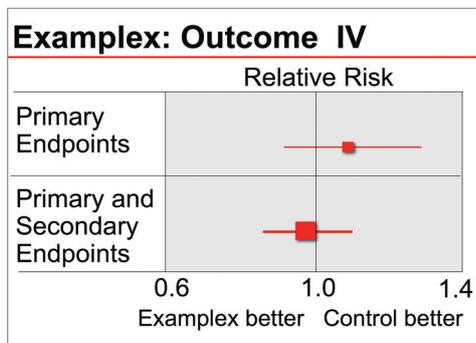
The Exemplix case study (cont)



The answer to a question for your statistician or medical advisor: ‘What are the statistical confidence intervals for these endpoints?’ will result in this diagram.



Asking your statistician or medical advisor ‘What are the results for primary and secondary endpoints in this study?’ results in this variation to the diagram.



Asking your statistician or medical advisor ‘How many of the individual data sets contribute to the primary and to the secondary endpoint?’ results in this diagram. The diagram has now shifted in favour of your product, although you cannot construe a clinically relevant difference between the two treatment arms. Is this a fair representation? Yes it is, because the combined number of primary and secondary endpoints is usually more relevant to practising physicians who see the patients in their medical practice

– independently of whether an endpoint met the required strict adherence to study protocol criteria which would qualify it as primary.

The Exemplix case study (cont)

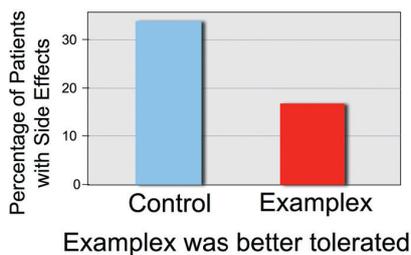
Exemplix: Message

Exemplix is effective in preventing cardiovascular complications:
An appropriate and safe initial treatment

The substance used as active control in this trial was standard treatment in the disease investigated. Prior clinical studies had clearly demonstrated it prevented cardiovascular complications. Since this trial found no relevant difference in efficacy between the active control and the substance Exemplix, Exemplix can be considered as having similar beneficial effects to the active control. This leads to the message expressed in the example.

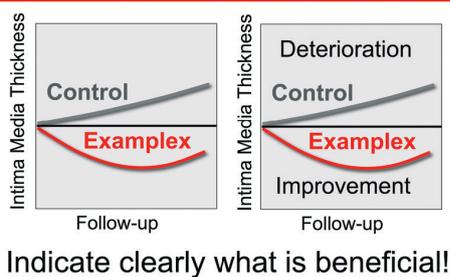
Be sure to discuss this with your medical department and check regulatory requirements in your country before promoting any message.

Exemplix: Side Effects



If the efficacies of your product and the active control are similar in your trial, check the profile of side effects. Exemplix has a better tolerability profile than the comparator.

Exemplix: 'Good or Bad'?



In some charts the increases or decreases of sonographic, radiological and laboratory parameters are not immediately apparent to the reader as a benefit or a disadvantage. You need to indicate clearly what is beneficial! The illustration shows one way to illustrate that the decrease in 'intima media thickness' associated with Exemplix is indeed a desirable outcome. Place the word 'improvement' on the appropriate side of the horizontal axis so that the reader instantly recognizes this change as a favourable result.

Sell the product not the study

Brand Name Visibility

Brand name in study name?

Eventually 'rename' the study
= Modify the study name

'Sell the product,
not the study'

Is your product mentioned in the name of the trial? What do you do if your brand name is not part of the study name? You could 'rename' the study internally so it reflects your brand name. In most cases, it is enough simply to put the product name before the study name (usually an acronym) when you refer to it. For example, the name of your product is 'Examplex' and the acronym of the study is 'ABC'. Your clinical trial name becomes the 'Examplex ABC study'. Make sure your team agrees to use the new term consistently in all your internal and external

material to ensure the biggest impact on prescribing behaviour.

A trial where the impact on sales of the substance investigated was very limited, was the HOT (Hypertension Optimal Treatment) trial – well known in the cardiovascular sector. However, only few prescribing physicians knew which was the main drug used in the trial (it was the calcium antagonist felodipine).

Know and respect statutory limits

Statutory Restrictions

Act responsibly and ethically:

Do **not** hide negative data!

Do **not** cover up negative results!

Publish **all** results whether positive or negative!

You should ensure compliance with all relevant standards. See chapter entitled 'Codes of Practice'. Your reputation and your credibility are your most valuable assets amongst your direct customers, the public and governmental agencies. Various incidents in late 2004 and early 2005 prompted government agencies to enact regulations that will require pharmaceutical companies to publish the trial results of all completed clinical trials that they have initiated. Companies that conceal trial results (for example, because they do not favour

their product) are providing a disservice to their customers and their product.

Handle 'negative data' appropriately

Handling 'Negative' Data

The company Eli Lilly will publish all of its clinical trial results on its clinical trial registry www.lillytrials.com

- Trial Results by Therapeutic Area
- Trial Results by Product
- Initiated Trials
- Recruiting Trials

One example for handling data from clinical trials is illustrated on the website www.lillytrials.com, where the company Eli Lilly will publish all of its clinical trial results. Visit this website to see how they do it.

Choose your words with care

Careless Wording

ABC & Co Training Document
Potential Questions about Product Safety



"... implying that sales reps were being taught to evade doctor's questions."

Based on a November 2004 article in The Wall Street Journal

Dictionary: to dodge = to keep away, to avoid

An article published in *The Wall Street Journal* commented on the use of the word 'dodge' in a company's training document that instructed sales representatives on how to deal with potential questions about the safety of their product. The training document could be interpreted as '... implying that sales representatives were being taught to evade doctors' questions.' The importance of responsible behaviour is obvious. In addition, be careful in your choice of words when writing your training manuals. Therefore watch what you write!

Beware careless emails

Careless Email

The Attorney ... filed civil fraud charges against the company, citing an e-mail written by company officials discussing ...

... the need to effectively manage the dissemination of data in order to minimize any potential negative commercial impact.

The Washington Post carried an article (26 August 2004) describing how the New York Attorney General Eliot L. Spitzer filed civil fraud charges against a big pharmaceutical company while citing an email in which company officials discussed certain studies and the need to manage effectively the dissemination of data in order to minimize any potential negative commercial impact. This incident shows how careless behaviour and careless emails can be loose cannonballs which can lead to legal proceedings against you and your company.