LEARNING WHICH REGULATORY STANDARDS ARE NON-STANDARD

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Types of Regulatory Standards

- Laws
- Regulations
- Guidelines
- Points to Consider
- Formal suggestions
- Informal comments

Laws & Regulations

- Hard to challenge or to ignore
- Discuss all planned deviations from the "official" path ahead of time with FDA or other agencies
- One's rationale must be very strong

Guidelines and Points to Consider

- Consider the definition of these terms
- Determine which do not make medical, scientific or logical sense for your product
- Determine if any are inappropriate or impractical guidelines or recommendations
- Determine if it is necessary to discuss the planned deviations ahead of time or not

Formal Written Suggestions or Recommendations from FDA

- Discuss the issues with them and try to convince them of your points
- Seek a compromise position that is a win-win and allows everyone to save face
- Determine if they are “wrong” or simply have a different perspective on the issue or question

Formal FDAWritten Suggestions From Minutes & Correspondence

- Determine the likely outcome of not following the agency's formal recommendation(s)
- Determine if it is advisable to appeal their decision now or whether to wait till later, perhaps to the FDA Advisory Committee
- Finally, decide on the course to follow and who will be the best people to employ

Appealing FDA Recommendations You Believe are LiterallyWrong

- Decide if you want to appeal yourselves or have a third party group (e.g., patient association) appeal for you
- Decide who to appeal to, and go in order up the ladder rather than skipping some people. They can make your ability to succeed more difficult (e.g., Division Director, Office Director) or go straight to the Ombudsman

Appealing FDA Decisions that Depend on One's Perspective or Judgment

- Try very hard to find a compromise position that allows everyone to save face
- Consider all of the previous interactions
- Consider appealing legal issues to the general counsel's office
- Think outside the bun to find a solution

Appealing FDA Recommendations that are Based on Personal Opinions and are Not Consistent with Those of Others in Other Reviewing Divisions

- Consider the techniques listed above
- Push for GRRPs whenever possible (Good Regulatory Review Practices)
- Appeals may be required
- Good Luck!!!

ICH's CTD

- The ICH CTD only standardized format of regulatory submissions
- The ICH did not address how regulatory agencies are to review applications
- That is the next step that an ideal process would follow, i.e., to achieve greater consistency within and between agencies

Examples Where Companies Do More Work Than Standards Require

- Monitoring large trials
- Collecting too much data on a single patient, at a single visit, having too many visits, or conducting too many trials
- Allowing procedure bloat to occur

Specific Regulatory Standards One May Question

- Use of surrogate endpoints (Subpart H)
- Amount of monitoring to do
- Number of well-controlled trials
- Number of dropouts allowed
- Number of patients required in the database
- Amount of toxicology data required
- Amount of PK data needed

Specific Regulatory Standards That May be Questioned

- Statistical approaches to issues, but be sure to do this before breaking the blind
- Clinical interpretations that are not in the mainstream of medical thought
- Interpretations that do not account for current thinking or theories
- Views that are impractical and unrealistic

Tips & Lessons

- Everyone wants to study everything in Phase IV—The FDA has heard it before
- "Our drug is very similar chemically to X so that we should not have to study as much toxicology" (or PK, or other aspects). Sure!
- Remember that an Orphan drug designation and $1.20 gets you on the Metro

Professionals Versus Amateurs

- In approaching the FDA are you approaching them as a professional or as an amateur?
- Are you going to be seen as an equal partner in development who will work out a fair and equitable agreement, or are you going to try to see what you can “get away with”
- Are you sticking to scientific arguments?

Approaches to the FDA

- Are you defensive or collaborative?
- What is the attitude you want to portray?
- Are your rationales based on science?
- Are you fully prepared and rehearsed?
- Do you really know your stuff?
- Can you negotiate positions effectively?
- Do you have several fall-back positions?

Why do you want to do less work than standards suggest?

- Great medical need
- Time it will take to get onto the market
- Rarity of patients to study
- Well established safety or efficacy

- HAVE YOUR DUCKS LINED UP TO PROVE THESE POINTS SCIENTIFICALLY & MEDICALLY

How Not to Prove Points

- Professors A and B state that ….
- We have seen some patients who…
- Most medical physicians feel that …
- The adverse event was only….
- The adverse event can be explained by…

Conclusions

- Be one of the professionals and seek to abridge standards only when you can justify the changes on a scientific and/or medical basis
- Don’t try to play games, but seek to have a level playing field where the agency is also not playing games

Conclusions

- Seek to work collaboratively with the FDA
- Seek to be a partner insofar as possible
- Remember your tone, as well as your words
- Be as creative as possible in developing your regulatory strategy
- Being creative will usually save time and money and lead to success