

Innovative Models of Compliance Education: *The Intellinex™ Case Study*

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Key Issues Facing the Pharma Industry

- Federal- OIG chief counsel makes it very clear that a major target in 2006 is evidence of off-label marketing
- Per James Sheehan, US Attorney's Office: Pharmaceutical fraud involving any major managed care plan or PDP (Medicare) – now a fraud/false claim on United States
- Senate Finance Committee asking for evidence of pharma spend on educational activities of all types
- Managed Care: several major carriers will not allow participation by medical affairs professionals in pharma-related activities, even CME
- State pressures:
 - *legislation increasing regarding accountability for gifts spending*
 - *California's SB 1765*
 - *Gov. Corzine (NJ) limiting faculty participation in pharma run events*

The Need

- Compliance training required by CIA (corporate integrity agreements) for many companies, plus general knowledge training.
- The need for quality in-house training for many pharma-related entities, i.e. vendors who perform med/com duties and meetings planning.
- Desire by senior compliance officers in pharma industry to develop a clear message for physician providers about the nature of these regulations

The Challenge

- How to keep dry material reasonably interesting !
- Translating complex concepts into practical knowledge for field force and vendors dealing with medical education
- Affordable vehicles for training that are flexible and readily changed as new regulatory issues surface
- Readily distributed via various forms of communication

The “New Learner”

Educational activities that use interactive techniques such as case discussion or hands-on practice sessions generally are more effective in changing behavior and patient outcomes which can result in changes to knowledge or skills...

E-learning Rationale

- Time-constrained environment
 - *Allows for quick-hit or “burst” learning™*
 - *Works for professionals of all types*
- Readily available technology via web, computer, mp3 and related devices
- Becoming more user-friendly
- Today’s learners looking for new options and creative solutions

Five benefits of E-learning

- **Learning benefits:** Making the whole learning experience more involving, faster and more effective
- **Distribution benefits:** Just-in-time delivery with just-enough content. Validation of usage and content understanding.
- **Content benefits:** Easier creation and updating of content allied to selective mass distribution.
- **Management benefits:** Improved facilities for monitoring learners, mentors and delivery. Improved monitoring of usage and performance makes learning more quantifiable.
- **Financial benefits:** These can be derived from all of the above. The promise of online learning is to reduce delivery costs and minimize time out from work.

On Demand Internet Module Training

(CardinalHealth Compliance “on-demand” module)

- User-friendly interface using Macromedia flash
- Narration option available
- Ongoing intramodule updates and refreshers to reinforce learning
- Testing component required- 80% minimum for passing
- Certificate of completion printable by employee
- Follow-up 1 hr small group “live” review with Dr. Lenow

CardinalHealth Compliance Training Solution

(a unique partnership with HCPPro and NXlevel)

Compliance
for CardinalHealth
SHS Employees

THE POWER OF ONE
STRATEGIC HEALTHCARE SOLUTIONS

Main Menu | About the Authors | Glossary | Help | Exit

- Introduction
- Welcome to Compliance for Pharma Sales
- What Is Compliance?
- Why Learn Compliance?
- Risks of Noncompliance
- Learning Objectives
- Enforcement
- Regulations
- Guidance
- Conclusion
- What Do You Know?

Why Learn Compliance?

As a sales rep, it's part of your responsibility to ensure compliance with the guidelines and relevant government regulations. By implementing a corporate compliance program, your organization has made a commitment to identify and prevent potential problems. When you have a compliance-related question, concern, or suggestion, look to your company's compliance program.

If you hold yourself accountable for understanding the rules and bringing questions forward, your organization will be accountable for responding to you and correcting situations before they become problems.



[Back](#) [Next](#)

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Intellinex^{TM*}

...for an enlightened future

Intellinex Case Strategy

- Elements can be used in a variety of formats
 - Live conferences
 - CD/DVD format for on-demand learning
 - Webinar formats
 - Short-form summary for supplemental discussion after more formal training sessions
- Formal ½ day conference combining audiences of pharma execs, med/com personnel from CardinalHealth, and students, residents and faculty from Jefferson Medical College
- Panel faculty from US Attorney Office, senior compliance counsel from BMS, Pfizer
- Interactive audience/faculty dialogue

Intellinex™ (generic: *telismarten*)

- from the **DREC** blockers class of drugs (Dunceiotensin Receptor and Enzyme Converted blockers),
- has the capabilities of improving human intelligence (per IQ measures) and project adherence and completion efficiencies.
- Intellinex™ is available in pill form as a once daily prescription (5, 10 mg and 20 mg doses; 10mg per 5ml, gelcaps, and capsule sprinkle formulations for the inept.

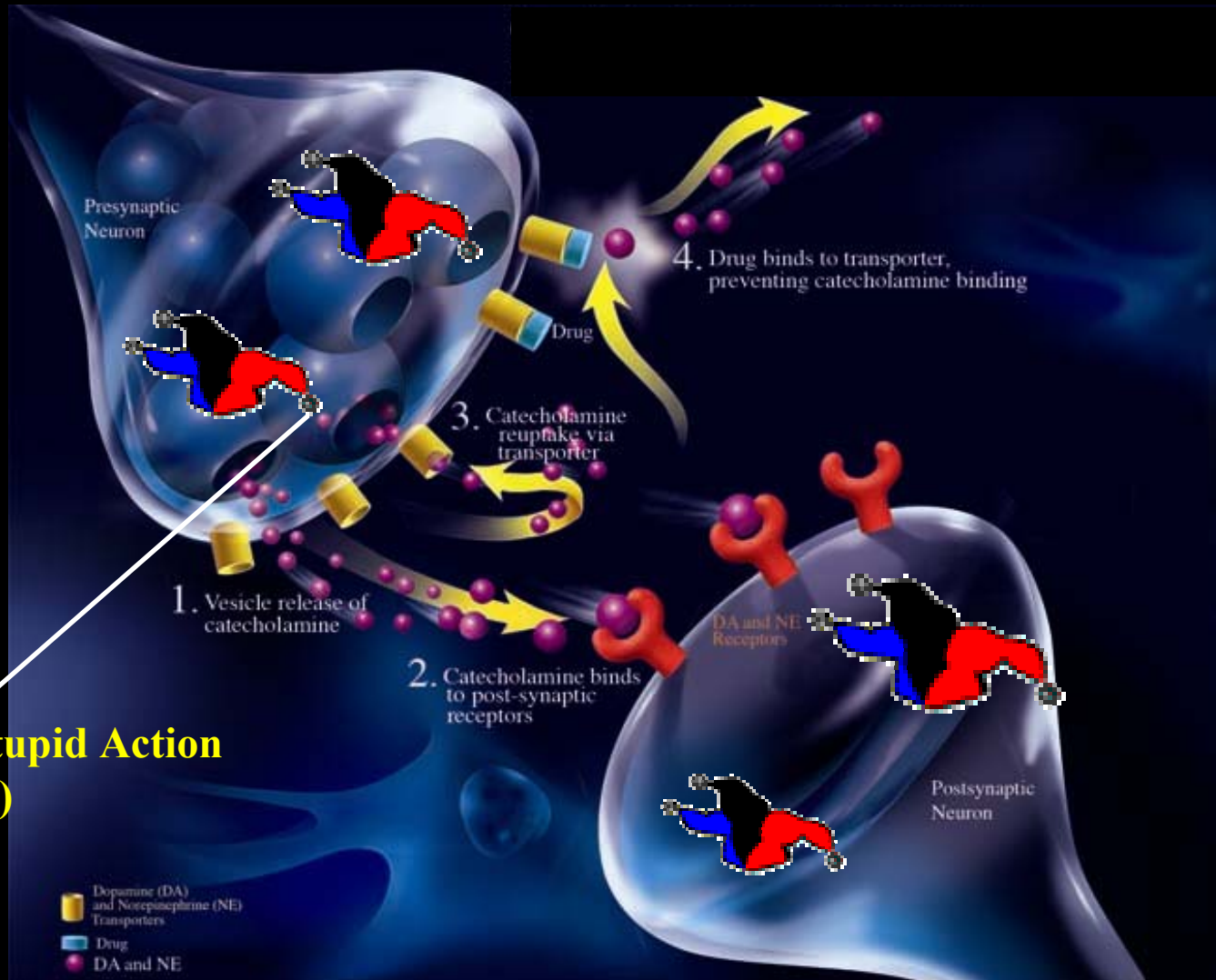
Labeled Indication

“Sudden Stupidness Syndrome (SSS) as manifested by an observed drop in one’s ability to answer the most basic questions; and for improvement in task performance in critical jobs affecting national security or important school exams”.

Pharmacology/MOA

- The mechanism of action is presumed to involve catecholamine reuptake inhibition (see MOA slide) though absolute MOA is still not completely understood.
- An additional mode of action postulated is to exert its therapeutic effect by enhancing cholinergic function.
- Test Labradoodles were demonstrated to improve chess-winning skills against mid-level Pharma management personnel (tenure of at least two years) to a success rate of 3 out of 4 (75%) games... this against the benchmark standard without drug enhancement of 2 out of 3 (66%) games, reaching checkmate on average of 2.4 moves faster than normal.

Catecholamine Reuptake Inhibition presumed Mechanism of Action of DREC blockers



(SAP; Stupid Action Potential)



Key Trials

- The **SMARTYPANTS** and **SMARTYPANTS II** trials involved over 4,500 study subjects who demonstrated an average of 13 points in IQ improvement on standard regimens of 10 mg daily during 12 week trials.
- **JETSMETSNETS** Trial (U.S), in which study subjects were not statistically significantly improved over placebo cohorts. In this trial of 600 New York sports fans, overall test results for simple tasks such as basic addition and third grade US History questions, on either 10mgs/day or placebo, were all well below expected values,...indeed, even for rocks.

Warnings Summary

- **Anesthesia:** Intellinex™ as a cholinesterase inhibitor, is likely to exaggerate succinylcholine-type muscle relaxation during anesthesia. Patients are also known to utter off - color phrases during induction.
- **Cardiovascular Conditions:** cholinesterase inhibitors may have vagotonic effects on the sinoatrial and atrioventricular nodes. This effect may manifest as bradycardia or heart block in patients both with and without known underlying cardiac conduction abnormalities. Syncopal episodes have been rarely reported with Intellinex™, usually collaterally by proud mothers who never thought their kids could be that smart!
- **Neurologic:** mild transient headaches have been reported with Intellinex™ which readily resolve upon cessation of the drug. However, then the parents get headaches from their whining children - so someone will probably still have a headache.
- **Pulmonary Conditions:** Because of their cholinomimetic actions, cholinesterase inhibitors should be prescribed with care to patients with a history of asthma or obstructive pulmonary disease. Duh!

Carcinogenesis/Fertility Issues

- No evidence of a carcinogenic potential was obtained in an 75-week carcinogenicity study of Intellinex™ conducted in CD-1 mice at doses up to 160 mg/kg/day (approximately 70 times the maximum recommended human dose on a mg/m² basis), or in a 123-week carcinogenicity study in Sprague-Dawley rats at doses up to 45mg/kg/day (approximately 40 times the maximum recommended human dose on a mg/m² basis).
- Additionally, Intellinex™ had no effect on fertility in Labradoodles at doses up to 115 mg/kg/day (approximately 9 times the maximum recommended human dose on a mg/m² basis). Of course, it was soon discovered that these test subjects had already been neutered thus rendering this particular value somewhat moot.

Drug History

- Developed by Javois Pharmaceuticals, Inc
- Originally designed for memory loss, side effect of “smartness”
- Needed large commercial partner with large field force, thus the relationship with **Devouré** Pharmaceuticals, Inc, in the United States
- Subsequent sales distribution relationship with McGuffin, Inc.

Drug History

- Same indications were approved by the FDA as was the case in Europe but the lower age limits were different.
- Age indication was originally 15 years of age and above, but due to strong yuppy parent lobbying from places like Moorestown, NJ; Gladwynne, PA and Silicon Valley, CA, the age was lowered to 13 years - the FDA review panel simply could not distinguish the symptoms of SSS from average onset of adolescence.
- Since the Phase III testing duration had not exceeded three months, the drug was approved for a maximum labeled indication of 12 weeks duration.

Marketing Campaign

- Expectations were exceedingly high and stock prices for **Devouré** were astoundingly inflated.
- The training for the agent had to be done very quickly and many sales personnel did not receive optimal preparatory training for the detailing of this agent.
- Budget for both promotional and especially CME programming were the highest in the industry.
- Aggressive DTC (direct to consumer) advertising would saturate the airwaves, print and cable/internet venues. This splash of media blitz preceded any physician/caregiver education and was simultaneous with medical publication advertising.

CE/CME (Continuing Education) Issues

- P. Patrick Purcell, aggressive product manager for Intellinex™, emphasized a very “hands on” approach to CME activity
- Retained *AnythingYouWant (AYW) Enterprises* as their CME vendor
- Purcell insisted on using certain “name” experts, which included several telismarten proponents who would likely be asked “off label” questions about the agent during “fair balanced” educational dinner meetings and satellite educational sessions at specialty meetings.

Appendix B

File	Edit	View	Insert	Format	Tools	Actions	Help					
Send	Print	Cut	Paste	Undo	Redo	Options...	Times New Roman	14	B	I	U	Text Alignment
To...	Intellinex product team											
Cc...	AYW Enterprises (Intellinex team)											
Subject:	CE (continuing education) meetings for caregivers/providers											

To: Intellinex CE Planning Group
From: PPurcell, Intellinex Product Mgr

My understanding from the **Devouré** regulatory review people is that there is nothing "formal" or binding in any of the OIG or pHRMA guidelines that mandate total separation of our product team people from CE support programming. Since **AnythingYouWant Enterprises**, our CE vendor, has responsibility under their own accrediting oversight entity, the ACCME, they have assured me that we can appropriately input into the process of CE strategy and that it is OK to ask us for input along the way.

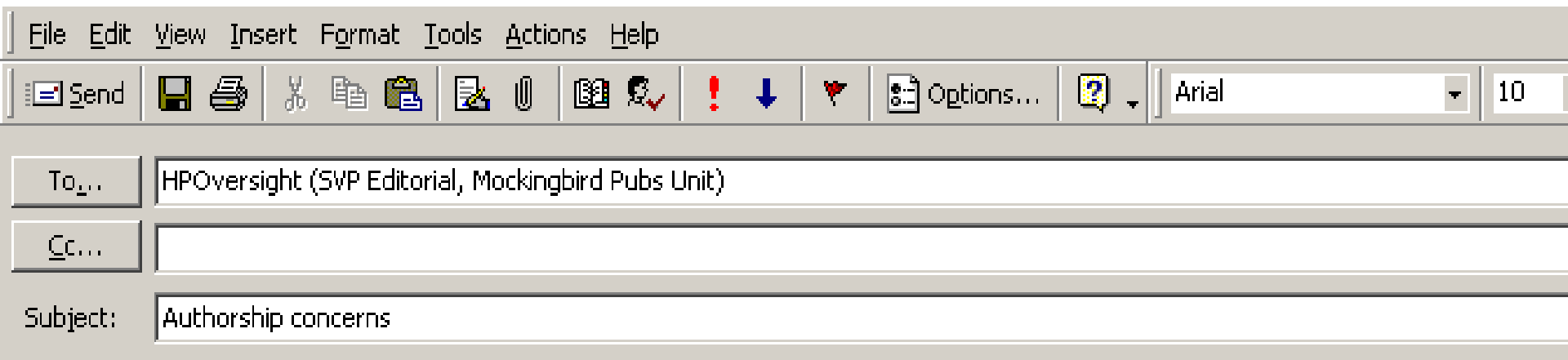
As the live programs are developed, I am particularly interested in Dr. Kids, our pediatric Key Opinion Leader from New Jersey, and his Nurse Practitioner, having a hand in the core slide deck and program style. They are HUGE supporters of ours and have great data on longer term use of Intellinex beyond the labeled indication of 12 weeks. Of course, our legal/regulatory people have mentioned that we can't promote such use in the field or any promotional activities generally. However, if questions just happen to get asked by dedicated and concerned providers out there about extended use of Intellinex, our speakers are certainly free to answer appropriately.

I encourage your creative input along the way. The volume of CE programming will be quite large this year, so no prescriber should be without an opportunity to gain this valuable training. Good luck. PP

The *Launch*

- DTC advertising hit the major television markets (national and cable), radio and internet venues.
- You couldn't miss the catch slogans such as: *“Who doesn't want a smarter kid™??”*
- Aggressive publications planning with short timelines and freelancers not well known to pubs planning unit
- Active hands-on role by product manager in CME planing as well as pubs process for promotion.

Appendix A



HP: with this deluge of new Intellinex business, I am a little concerned about our ability to properly manage the adherence to guideline protocols for author signoff and oversight. Some of these new freelancers are used to doing things a little differently and have not been as accountable as we normally hold our own writers. On the Journal of Irreproducible Results submission, for instance, Dr. Rubberstamp seemed too willing to sign off on a first draft. I spoke to him briefly, and I just have the sense that his overall involvement is not what it could be...please advise.

Launch Tactics

- Aggressive promotional dinner meeting focus- no pressure to leave out spouses, pretty lavish venues for meetings
- Hot giveaway was the Waterman logo Pen
- Some early concerns about slogan *“Who Doesn’t Want a Smarter Kid™”?* as potentially misleading
- Big push for samples and vouchers.

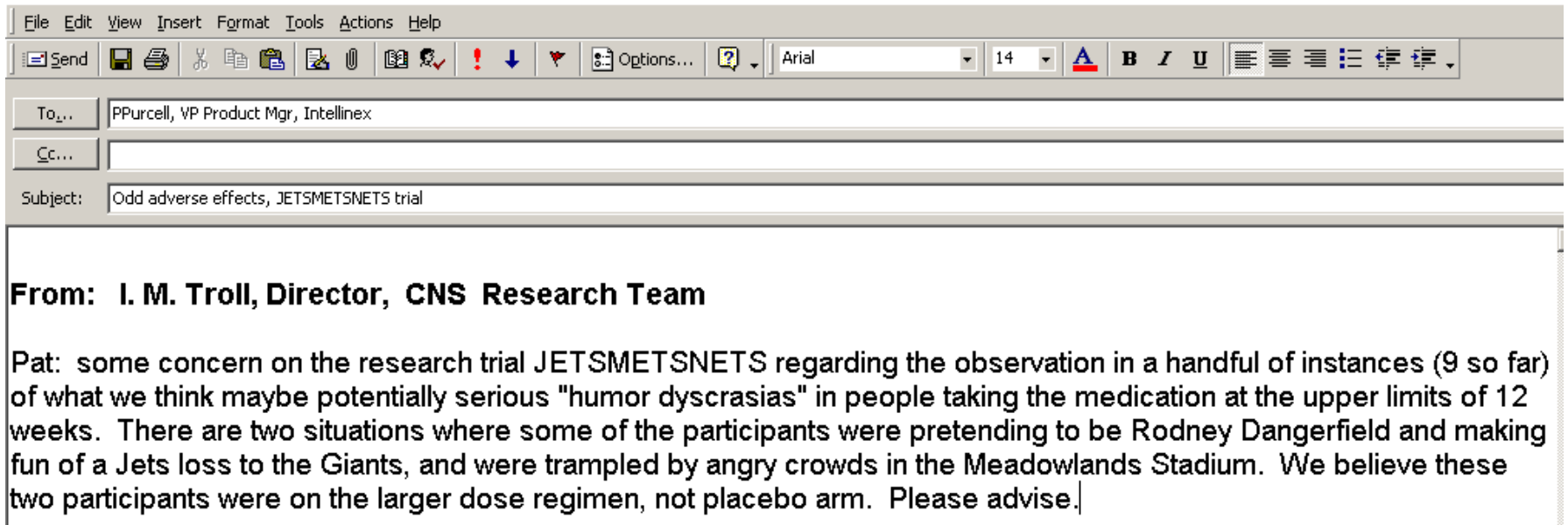
Black Box Warning

Use of Intellinex™, telismarten, beyond 12 weeks duration can lead to severe life threatening humor dyscrasias; and should especially be used with great caution if a New York Jets, Mets, or Nets fan

Black Box History/ Humor Dyscrasias

- About ten months into the US launch there were several anecdotal complaints about a somewhat rare side effect now categorized as “**humor dyscrasias**”.
- Several accounts of patients suddenly acting out in inappropriate settings, trying to be funny at funerals for instance, and doing routines often seen in entry-level comedy clubs were associated with use of this Intellinex™.
- Not identified in European trials and largely discounted by the **Devouré** team; indeed readily reversible effects

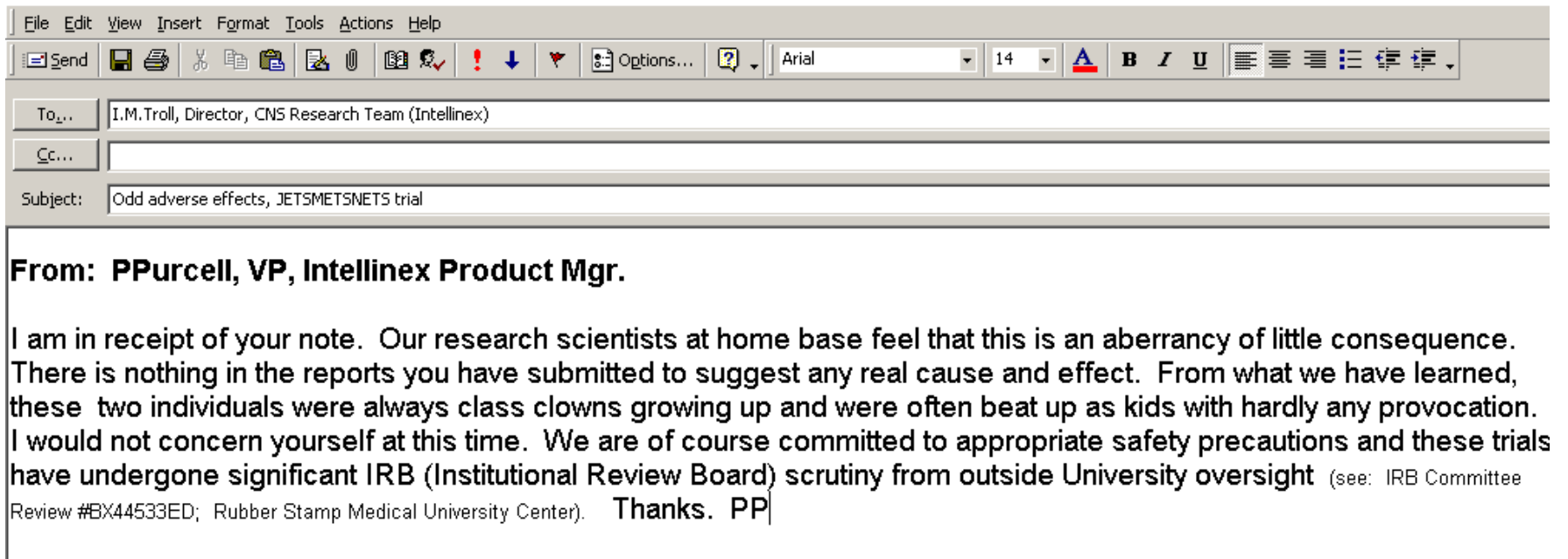
Appendix C



The screenshot shows an email client window with a menu bar (File, Edit, View, Insert, Format, Tools, Actions, Help) and a toolbar with icons for Send, Print, Copy, Paste, Undo, Redo, Bold, Italic, Underline, and text alignment. The email header shows the recipient as 'PPurcell, VP Product Mgr, Intellinex' and the subject as 'Odd adverse effects, JETSMETSNETS trial'. The main body of the email contains the following text:

From: I. M. Troll, Director, CNS Research Team

Pat: some concern on the research trial JETSMETSNETS regarding the observation in a handful of instances (9 so far) of what we think maybe potentially serious "humor dyscrasias" in people taking the medication at the upper limits of 12 weeks. There are two situations where some of the participants were pretending to be Rodney Dangerfield and making fun of a Jets loss to the Giants, and were trampled by angry crowds in the Meadowlands Stadium. We believe these two participants were on the larger dose regimen, not placebo arm. Please advise.



The screenshot shows a reply email in the same email client interface. The header shows the recipient as 'I.M.Troll, Director, CNS Research Team (Intellinex)' and the subject as 'Odd adverse effects, JETSMETSNETS trial'. The main body of the email contains the following text:

From: PPurcell, VP, Intellinex Product Mgr.

I am in receipt of your note. Our research scientists at home base feel that this is an aberrancy of little consequence. There is nothing in the reports you have submitted to suggest any real cause and effect. From what we have learned, these two individuals were always class clowns growing up and were often beat up as kids with hardly any provocation. I would not concern yourself at this time. We are of course committed to appropriate safety precautions and these trials have undergone significant IRB (Institutional Review Board) scrutiny from outside University oversight (see: IRB Committee Review #BX44533ED; Rubber Stamp Medical University Center). Thanks. PP

The Whistleblower

- Dr. Lancelot (CMO for **Devouré**) was uncomfortable with dyscrasia data and was ultimately able to discover confidential communications that tied the more severe humor dyscrasias to extended use of the drug beyond the labeled recommendation.
- **Devouré** retaliated with menial duties and reprimands
- Lancelot reports concerns to the OIG (Office of the Inspector General)
- Forced to sell prized Jaguar

Appendix D



MEMORANDUM

TO: CNS Research and Investigation Unit, Director
FROM: Team Leader, Trial Studies
RE: Long term use, telismarten

We have received a handful of anecdotal accounts, some from the JETSMETSNETS trial and now some reports from European follow up from the SMARTYPANTS II trial, as well as some calls from practitioners in the field (about 32 documented instances) of serious behavioral aberrations on the order of what may be advanced humor dyscrasias in patients on long term use of the agent, i.e. beyond 26 weeks. Seems from what has been ascertained thus far, that these quickly reverse on cessation of the medication and usually associated with the larger dose of 20 mg and higher. While the JETSMETSNETS trial example was two serious cases which have been alternatively explained, we cannot dismiss so readily the accounts called in by these practitioners. The numbers are still small statistically against the millions of unaffected users, but probably something we need to watch more closely. Perhaps this should be shared with the product management executive team and the regulatory folks? None of these practitioners has filed any observed instances with any regulatory agencies as yet, as they were uncertain as to the likely cause of these behaviors.]

Repercussions

- Senator Weedy of Iowa calls Senate Finance Committee hearings
- OIG brings legal action
- **Devouré** agrees to CIA (Corporate Integrity Agreement) settlement of over \$800 Million
- Dr. Lancelot receives \$24 Million for his reward

Summary

- **Devouré** has quietly begun research in cooperation with another partner and with Javois, Inc. to determine racemic isomeric variations on telismarten such to extend patent life in the years ahead
- Is funding research on extended use of the telismarten beyond the original 12 week indication.
- Mr. Javois has purchased his own Caribbean island where he employs only very smart elderly servants.
- Labradoodles now sell for \$10,000 each if you can get one from the Purcell Doodle Ranch.

Pros and Cons of Case-based Model

- Enjoyable change of pace and diversion for learners
- Engages learners much more
- Creates an interest in debate and ongoing follow-up sessions
- Feedback uniformly positive when well constructed
- Makes “dry” material more appealing
- Commitment at top a must
- Time consuming to prepare-typically 5:1 compared to traditional curricula
- Requires expert facilitation, someone who “knows” how to do this well
- Some risk if audience is not equipped for this type of educational approach