HYPOTHETICAL SCENARIO: MINI SUMMIT II: R&D COMPLIANCE

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This hypothetical is entirely fictitious. Any resemblance to actual companies, individuals, or products is unintended and coincidental.

Portera Pharma

- Portera Pharma is a mid-sized, oncology-focused pharmaceutical company that was founded in 1980.
  - They have several approved orphan drug products, and ongoing development programs for kidney and bladder cancer.
- Two years ago they settled a U.S. kickback- and off-label-focused investigation relating to the activities of prior Marketing/Sales management, Medical Affairs activities related to IISs, and MSL interactions with HCPs.
  - As part of the $55M settlement, they signed a CIA that includes an array of controls relating to payments to HCPs, healthcare institutions, investigators, and promotional activities.
  - Costs associated with the settlement and a drop in sales have made it difficult for Portera to fund its pipeline development program.

U.S. Kidney Cancer Trial

- Portera is conducting a Phase III U.S. kidney cancer trial of their drug Porterine as part of a joint venture with Research Equity, a CRO/investment firm hybrid.
  - There are 75 sites enrolling 750 patients.
- Portera provided $10M in start up costs for Research Equity to conduct the trial, with the rest of the payments to Research Equity based on milestones associated with rapid enrollment and execution of the trial, and a royalty on Porterine sales based on the successful outcome of the trial and ultimate approval.
- Research Equity is implementing a risk-based monitoring plan for the trial, and Portera is provided regular dashboard reports on key performance indicators. Portera also has auditing rights.

True or False?

- The CEO of Portera is glad that they have outsourced this work to Research Equity. This means he can get research done quickly and efficiently without worrying about their CIA.
- False – Research Equity is likely to be considered a “third party” covered by the CIA, since the CIA includes research activities with investigators. Also, Portera has audit rights, and has contributed $10MM to the research. Although outsourced, Portera remains the overall accountable party for this research and its oversight.

True or False?

- The royalty payment to Research Equity does not raise any compliance concerns, because Research Equity is not a health care professional or institution.
- False. Without careful monitoring by Portera, the royalty could incentivize Research Equity to take shortcuts in order to get the drug commercialized faster. This could include compromises on payments to investigators or sites, or lack of attention to adverse events or quality concerns.

U.S. Kidney Cancer Trial (cont'd.)

- On a regular call with Portera several weeks into the trial, Research Equity reports that they are getting requests from sites asking them to pay for co-pays for trial subjects for various procedures and drugs used in the overall course of treatment.
  - Obstacles to payment have been slowing enrollment.
  - The sites report that a competing trial sponsor is already paying such costs

What Do You Think?

Portera's clinical team should tell Research Equity to:

A. Pay the copays - it's the ethical thing to do for subjects – that's why other companies are doing it;

B. Pay the copays - enrollment will stall and patients may never see the drug come to market;

C. Not pay the copays – Finance says Portera doesn't have the money to fund copays;

D. Not pay the copays – their lawyers say this is a potential violation of public and private insurance laws.

U.S. Kidney Cancer Trial

- Eight months into the trial, Research Equity reports that they had just discovered that one of the investigators at a site in Ohio had been excluded from government healthcare programs 20 years ago for a conviction relating to drug possession.
- The investigator apparently went through a treatment program, had his medical license reinstated, and has been practicing without incident since that time. The institution where he currently works was not aware of his exclusion and has an investigation underway.

Compliance Officer: What Would You Do?

A. Immediately terminate the site – Research Equity, as Portera's agent, should not be contracting with anyone who had been excluded or debarred for any reason.

B. Review the investigator's qualifications, but probably terminate – the appearance of impropriety is enough to taint the research. Also revise your company's procedures for detecting a history of exclusion or debarment.

C. Review the investigator's more recent qualifications and track record in his field and in research. It is probably OK to keep the site and investigator after consideration the facts and circumstances of the exclusion, given the passage of time and his clean record. Also revise your company's procedures for detecting a history of exclusion or debarment.

D. None of the above – do something else (tell us what you think?)

U.S. Kidney Cancer Trial (cont'd.)

- In an audit conducted after the trial and just prior to submission of the NDA for the product, Portera discovers that at least two sites double-billed for protocol-required services for study subjects (i.e., billed both the CRO/Sponsor and the government).

Portera Compliance: What Would You Do?

A. Tell the sites about your findings, report the sites immediately to the OIG, and terminate the sites from the study;
B. Tell the sites about your findings. If they take appropriate action (e.g., self-disclosure to OIG or other similar action) keep them as active sites;
C. Tell the sites about your findings and immediately terminate them from the study;
D. None of the above – something else (tell us what you think)

U.S Kidney Cancer Trial (cont'd.)

- In the audit, Portera also finds that information collected by Research Equity on investigator financial interests, required for submission of the NDA under 21 CFR Part 54, appears to be inconsistent with Portera's Open Payments disclosure of payments made to some of those investigators for various consulting, speaking, and advisory board activities relating to approved and pipeline Portera products.

Portera Compliance: What Do You Think?

A. It's OK; no one checks the FDA financial conflicts forms anyway;
B. It's not OK; go back to the investigators to reconcile the payment information.
C. It might be OK, since the standards for FDA conflicts reporting and for Open Payments may differ. Check the details and assure yourself that you are comfortable with the discrepancies;
D. None of the above – something else (tell us what you think).

U.S. Kidney Cancer Trial (cont'd.)

- At another site, which had been the subject of a monitoring visit by Research Equity, Portera finds a major discrepancy in records of study subject follow up exams, which were required to be conducted at specific intervals.
  - It appears that at least 10 subjects had exams on the same day.
  - The records are suspiciously identical, and there is no record of an investigator being on-site that day

What Do You Think?

Portera's clinical team research should:

A. Wrap-up the monitoring in a timely manner and document this site situation for future consideration / site selection

B. Open up an investigation under Portera's R&D investigations SOP and – depending on the outcome, consider any necessary external reporting and exclusion of site data

C. Discuss with data management how to best address these one-off data issues to expedite database lock and reporting

D. Consider auditing Research Equity

Ming Bio

- Portera is negotiating a joint venture with Ming Bio.
  - Based in Shenzhen, China, Ming Bio has developed a promising compound – Mingabine -- for treatment of bladder cancer.
  - Under the potential joint venture, Portera would get rights to Mingabine in the U.S. and EU.
  - The owners of Ming Bio have extensive connections with the Chinese government, and Portera is hoping the venture will also facilitate the conduct of a major planned trial of Porterine in China. If the trial is successful and the product is approved, the joint venture – MingPortera – would market Porterine, and potentially other Portera products, in China.

What are some steps you might want to take?

A. Do a media search on Ming Bio and its principals in all news sources available to Portera. They have subscriptions to The Washington Post and the New York Times. That should give you a good idea about whether Ming Bio is a reputable company.

B. Engage a US law firm to have an associate in NY do a media search and some “due diligence” on Ming Bio and its principals.

C. Engage an outside law firm or consultant based in China to do due diligence on the principals of Ming Bio, their relationships with government officials, and the company’s compliance history.

D. Don’t worry about it too much. If the Chinese government thinks Ming Bio is a good company to work with, it probably is.

Ming Bio (cont'd.)

- Ming Bio has conducted a major trial of Mingabine, showing impressive results. Most of the sites were in China, but about 20 percent of the sites were in Latin America and Eastern Europe.
- To attract investigators in Eastern Europe and Latin America, Ming Bio held its investigator training at the Ritz Hotel in Paris during the European Bladder Cancer Conference.
- In order to facilitate rapid enrollment, Ming Bio has paid sites throughout China special bonuses for meeting enrollment targets.

Any issues here?

A. No, because the potential investigators were at the conference anyway so it was fine to invite them to the Ritz, and bonuses for fast enrollment are not against the law.
B. No, because meeting and bonuses will help to speed development of this promising potential therapy for cancer.
C. Yes – review the nature of the bonuses and trips and whether they raise corruption issues and/or introduced bias into the conduct of the study, raising data integrity issues.
D. None of the above – something else (tell us what you think)