

AMP Professional Relations Annual Report (11-2010 through 11-2011)

PRC Members: Members for this committee are Elaine Lyon (Chair), Roger Klein (Chair-elect), Jean Amos Wilson, Vicky Pratt, Jan Nowak, Tim O’Leary, Roberta Madej, Shelby Melton, Andrea Ferreira-Gonzalez, Daniel Sabbath, Stephen Day, Rajyasree Emmadi, Daniel Farkas, Robert Klees and Iris Schriver (President-elect). The committee reflects representation from a variety of scientific, institutional and commercial backgrounds.

The AMP Professional Relations Committee is the primary liaison between AMP and other organizations. Major responsibilities of the Committee include: 1. Communicating and coordinating activities with the appropriate government, patient, and professional organizations to inform policy discussions that influence the practice of molecular pathology, 2. Developing AMP positions on emerging issues affecting molecular pathology, 3. Interacting with a wide variety of entities, including other professional associations, Congress and U.S. Federal Agencies such as FDA, CDC, DHHS.

Department of Health and Human Services:

The PRC prepared a response to the advanced notice of proposed rule-making by the Department of Health and Human Services “**Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators.**” AMP commended the agency on its efforts to streamline the regulations governing human research protections and allowing a multi-site study to use a single IRB. However, AMP has some concerns and made the following requests. 1. AMP is concerned that all biospecimens may be considered identifiable and encourages regulators to consider a more practical approach. 2. We request that the rule include language that clearly identifies using samples for validation or verification are quality control and quality assessment activities rather than research to prevent misinterpretation.

AHRQ:

We provided comments to the Agency for Healthcare Research and Quality on the draft Technology Assessment (TA), **Update on Horizon Scans of Genetic Tests Currently Available for Clinical Use in Cancers.** In summary, we commented on their broad use of the term “genetic”, requested authors to consult with subject matter experts prior to finalizing the report, requested that tests be described based on their molecular entities rather than using brand names, and requested that the TA be modified to distinguish between test manufacturers and clinical laboratories developing LDTs. In August, we also met with Dr. Gurvaneet Randhawa, the agency’s Senior Advisor on Clinical Genomics & Personalized Medicine, to continue this conversation.

NIH:

The PRC responded to the request for comments regarding the **Genetic Test registry**. The main points are summarized below. 1. The format as proposed includes levels of details that may result in confusing information. The GTR should differentiate between the data elements for manufacturers, research and clinical laboratories. Some data elements address detailed issues of laboratory policy that are inappropriate for inclusion in the GTR and raise legal and liability concerns. Some data fields request information that is not relevant or useful for the purposes of the GTR. 2. The NIH has grossly underestimated the burden to provide the information as to the average number of submissions per respondent, the estimated time for submission, and the mean hourly wage for data entry. In addition, no burden estimate is included for updating the Registry as tests are improved. 3. AMP recommends several ways to minimize the burden for those submitting data such as a centralized, online location for test developers, manufacturers, and researchers, and information such as clinical validity and utility that are not laboratory-specific, but will be common among all laboratories need to be addressed in a centralized manner using materials from experts in the field.

FDA:

Meetings: In November, 2010, AMP participated in a coalition of nine professional organizations in a full-day meeting on the **Regulation of LDTs**. This meeting discussed the following topics: What constitutes an LDT? How can unique advantages of an LDT continue within FDA regulation?; Registration and Listing – Forum to discuss various alternatives to registering clinical laboratories as a medical device manufacturer and listing LDTs; and FDA Regulation of LDTs in a CLIA Framework - Forum to discuss the overlaps, gaps and possible efficiencies. PRC members **Vicky Pratt**, **Andrea Ferreira-Gonzalez** and **Elaine Lyon**, and AMP's **Mary Williams** participated in panel discussions.

In June 2011, the FDA hosted a public meeting on “**Ultra High Throughput Sequencing for Clinical Diagnostics Applications – Approaches to Assess Analytical Validity**”. AMP gave both written and oral comments. AMP's main points were 1. The FDA needs to partner with professional associations; 2 Different standards are needed for different types of applications; 3. Some aspects of analytical validity fall within the practice of medicine; 4. The FDA needs to review the analytical validity and bioinformatics together and separately.

Responses to FDA draft guidance documents: The PRC prepared responses to a number of FDA draft guidance documents. The document and summary of AMP's points are listed below.

‘Establishing the Performance Characteristics of *In Vitro* Diagnostic Devices for the Detection of *Clostridium difficile*’

AMP expressed concern that the guidance document may increase the cost of assay development and that some of the new requirements may not be necessary to develop high quality assays. We asked for clarification on cross-reactivity, confirmatory testing and study design.

‘Establishing the Performance Characteristics of Nucleic Acid-Based *In Vitro* Diagnostic Devices for the Detection and Differentiation of Methicillin-Resistant *Staphylococcus aureus* and *Staphylococcus aureus*’.

AMP requested clarification of the focus of the document, (e.g. test systems or specific assays). Further, AMP requests that the FDA provide additional clarity on the types of clinical performance data required for an application, as the descriptions of data requirements for analytical and clinical performance are conflicting.

‘Commercially Distributed *In Vitro* Diagnostic Products Labeled for Research Use Only or Investigational Use Only: Frequently Asked Questions’.

To avoid the disruption of patient care, AMP asked the FDA carefully to consider enforcement discretion or alternative regulatory pathways to address circumstances where no FDA cleared/approved products are available, particularly for those products with limited sales volume. AMP gave several recommendations, including 1. Direct enforcement requirements for 510(k) or PMA submissions toward test kits and test systems. 2. Create a consistent and clear pathway to encourage and facilitate ASR, 510(k) or PMA applications for RUO and IUO products, with a reasonable compliance timeline. 3. Accommodations should be made to enable certain reagents such as primer or probe mixes to be sold as ASRs; 4. Clearly state the scope of the guidance.

‘*In Vitro* Companion Diagnostic Devices’

AMP developed a position statement entitled “**Reference to Diagnostic Tests in Drug Labels**” that is available on the website. We sent a letter to Janet Woodcock, MD, Director for the Center for Drug Evaluation and Research re-stating our position. Our main point is as follows: **To promote patient safety and high quality care, AMP respectfully asks FDA to specify that diagnostics be described by the biological description of the gene or mutation on drug labels and that identification of recommended diagnostic testing not be by brand name.** We were pleased that our recommendation was included in the FDA’s draft guidance; however, there were other concerns that the PRC addressed in its written comments. We reiterated that FDA’s primary focus should be the companion biomarker rather than specific tests to measure it. We commented on the following points: 1. FDA’s policy of limiting approval of novel therapeutic products linked to biomarkers to those for which an FDA cleared or approved assay is available is too restrictive. 2. Reflexive classification of tests for companion biomarkers as high risk may impede the commercial development of new assay and the advancement of new test methods. 3. Final determination of significant risk for the

purposes of compliance with IDE regulations should primarily be made by the institutional review board overseeing the study. 4. Pharmaceutical and diagnostic sponsors should be required to provide data on the negative predictive value of a test used to predict drug or biologic responsiveness. 5. Pharmaceutical and diagnostic sponsors should be required to submit studies of all assays for companion biomarkers for peer reviewed publication.

CMS:

In July, AMP attended the public meeting on determining pricing for the Clinical Lab Fee Schedule. CMS decided to defer the addition of the newly formed codes for genetic tests for at least a year and instead, held a listening session on the topic. While the EAC took the lead on this issue and in the public comments, the PRC plans to meet with CMS in the future to discuss reimbursement policy including PhD billing.

Capitol Hill:

We continued educating congressional staff members in the House of Representatives and the Senate, focusing on issues relating to DNA patents, standardized reference materials, regulation of LDTs, and PhD billing. AMP spent numerous days on the Hill and met with more than twenty offices.

DNA patents:

We worked with Congresswoman Debbie Wasserman Schultz's (D-FL) staff on her amendment to H.R 1249, the America Invents Act, a comprehensive reform to the US patent system. The intent of the amendment was to allow testing of patented genes for the purpose of obtaining second opinions; however, the language included so many exceptions and loopholes that it failed to reach this goal and actually reinforced the patents. Fortunately, this language was removed, thanks to the great efforts of Mary Williams and Jennifer Leib, and replaced with a study to investigate the effects of gene patents on access to testing. The bill has passed both the Senate and the House, and was signed into law by President Obama. During the debate on the Senate floor, Senator Patrick Leahy stated that this legislation does not imply Congressional support for or against the gene patent case, and in doing so, mentioned AMP. And, AMP's name is now officially part of the *Congressional Record* for this vote.

LDT regulation:

We've met with congressional and senate office to discuss FDA oversight of LDTs: We shared AMP's main concerns with FDA oversight as being 1. Defining risk, 2. Labeling our services as "device manufacturers" rather than "health care professionals", 3. Having oversight from two regulatory bodies, CLIA and FDA. We are in discussions with The American Clinical Laboratory Association (ACLA) regarding the possibility of introducing legislation to clarify that LDTs remain under an enhanced CLIA rather than under the FDA. We recently received

legislative language on a CLIA-centric model introduced by Rep. Burgess (R-TX) that the PRC is reviewing for content.

International:

AMP has been invited to attend an international workshop on the regulation of Genetic Testing in Leuven, Belgium, organized by the EuroGentest network. The workshop will bring together a full range of stakeholders including clinicians, scientists, industry, patient/consumer groups and policymakers. Participants include representatives from the European Commission, FDA's Office of In Vitro Diagnostics, and European Diagnostic Manufacturers Association, to name a few.