DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Center for Environmental Health/Agency for Toxic Substances and Disease Registry

The Health Department Subcommittee of the Board of Scientific Counselors (BSC), Centers for Disease Control and Prevention (CDC), National Center for Environmental Health (NCEH)/Agency for Toxic Substances and Disease Registry (ATSDR): Teleconference Meeting.

In accordance with section 10(a)(2) of the Federal Advisory Committee Act (Pub. L. 92–463), the Centers for Disease Control and Prevention, NCEH/ATSDR announces the following subcommittee teleconference meeting:

Name: Health Department Subcommitteee

Time and Date: 1 p.m.–2:30 p.m., October 16, 2006
Place: Century Center, 1825 Century Boulevard, Atlanta, Georgia 30345.
Status: Open to the public, teleconference access limited only by availability of telephone ports.
Purpose: Under the charge of the Board of Scientific Counselors, NCEH/ATSDR the Health Department Subcommittee will provide the BSC, NCEH/ATSDR with advice and recommendations on local and state health department issues and concerns that pertain to the mandates and mission of NCEH/ATSDR.

Matters To Be Discussed:
The meeting agenda will include a follow-up on Workforce Recommendations; a selection of FY 2007/2008 Environmental Public Health Program Priorities; and the next steps for the Health Department Subcommittee. Items are subject to change as priorities dictate.

Supplemental Information: This teleconference meeting is scheduled to begin at 1 p.m. Eastern Standard Time. To participate during the Public Comment period (2–2:10 p.m. Eastern Standard Time), dial (877) 315–6535 and enter conference code 383520.
For More Information Contact: Individuals interested in attending the meeting, please contact Shirley D. Little, Committee Management Specialist, NCEH/ATSDR, 1600 Clifton Road, Mail Stop E–28, Atlanta, GA 30333; telephone (404) 498–0003, fax (404) 498–0059; E-mail: sittle@cdc.gov.
The Director, Management Analysis and Services Office, has been delegated the authority to sign Federal Register notices pertaining to announcements of meetings and other committee management activities, for both CDC and the Agency for Toxic Substances and Disease Registry.


Alvin Hall,
Director, Management Analysis and Services Office, Centers for Disease Control and Prevention.

For More Information Contact: Submit written or electronic comments by November 27, 2006.

ADDRESS: Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.fda.gov/dockets/ecomments.

FOR FURTHER INFORMATION CONTACT: Suzanne O’Shea, Office of Combination Products, 15800 Crabbs Branch Way, suite 200, Rockville, MD 20855, 301–427–1934, FAX: 301–427–1935, e-mail: suzanne.oshea@fda.hhs.gov.

SUMMARY:
The Federal Food, Drug, and Cosmetic Act (the Act) requires that the agency is to consult with stakeholders and the directors of the agency centers. After such consultation, OCP is to determine whether to continue in effect, modify, revise, or eliminate such an agreement, guidance, or practice, and publish in the Federal Register a notice of the availability of any modified or revised agreement, guidance, or practice.

This notice provides the preliminary results of OCP’s review of agreements, guidances, and practices that were in effect at the time section 503(g)(4)(F) of the act was enacted for their consistency with the act’s requirement for the prompt assignment of combination products to agency centers on the basis of the products’ primary mode of action (PMAO). The directors of relevant

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Review of Agreements, Guidances, and Practices Specific to Assignment of Combination Products in Compliance With the Medical Device User Fee and Modernization Act of 2002; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Federal Food, Drug, and Cosmetic Act (the Act) requires the Food and Drug Administration (FDA) to review each agreement, guidance, or practice that is specific to the assignment of combination products to agency centers and to determine whether the agreement, guidance, or practice is consistent with the requirements of section 503(g) of the act. In carrying out such a review, OCP is to consult with stakeholders and the directors of the agency centers. After such consultation, OCP is to determine whether to continue in effect, modify, revise, or eliminate such agreement, guidance, or practice, and publish in the Federal Register a notice of the availability of any modified or revised agreement, guidance, or practice.

This notice provides the preliminary results of OCP’s review of agreements, guidances, and practices that were in effect at the time section 503(g)(4)(F) of the act was enacted for their consistency with the act’s requirement for the prompt assignment of combination products to agency centers on the basis of the products’ primary mode of action (PMAO). The directors of relevant
agency centers have been consulted in this review. The agency now seeks

stakeholder comment with respect to the following issues: (1) Whether the

agency has identified all agreements, guidelines, and practices specific to the

assignment of combination products that should have been included in this

review; (2) whether the agency’s

conclusions regarding the consistency of

the agreements, guidelines, and practices with the act’s requirement that

combination products be assigned promptly based on their PMOA is

accurate; and (3) whether the identified agreements, guidelines, and practices

should be continued in effect, modified, revised, or eliminated.

Upon receipt and review of stakeholder input, the agency will

publish another Federal Register notice

announcing its determinations and the

availability of any modified or revised

agreements, guidelines, or practices.

II. Primary Mode of Action—The

Principle Underlying the Assignment of

Combination Products to Agency

Centers

Section 503(g)(1) of the act requires that

combination products be assigned to a lead agency center based upon the

agency’s determination of the product’s

PMOA. The agency published a final

rule defining the PMOA of a

combination product in the Federal

Register of August 25, 2005 (70 FR

49848), after consulting with directors of the relevant agency centers and other

agency officials, and obtaining

stakeholder input through notice and

comment rulemaking. As defined in the

regulation, a combination product’s

PMOA is its single mode of action that

provides the most important therapeutic

action of the product (§ 3.2(m) (21 CFR

3.2(m))). The regulation includes an

algorithm that will be followed when the

most important therapeutic action of a

combination product cannot be
determined with reasonable certainty

(§ 3.4(b)). The regulation is intended to

promote the public health by codifying the

agency’s criteria for the assignment of

combination products in transparent,

consistent, and predictable terms. The

regulation went into effect on November 23, 2005. A copy of the final rule is

available at http://www.fda.gov/

OHRMS/DOCKETS/98fr/05-16527.htm.

III. Agreements and Guidelines Specific to the Assignment of Combination

Products

The agency has identified the three

intercenter agreements (ICAs) as the

agreements or guidelines specific to the

assignment of combination products

described in section 503(g)(4)(F) of the

act. The three ICAs were entered into in

1991 by the Center for Biologics

Evaluation and Research (CBER), the

Center for Drug Evaluation and Research (CDER), and the Center for Devices

and Radiological Health (CDRH) shortly after Congress introduced the concept

of combination products in the Safe Medical Devices Act of 1990 (SMDA).

Although the three ICAs (i.e., the CDER–CDRH ICA, the CBER–CDER ICA, and

the CBER–CDRH ICA) differ in content, format, and scope, they are all specific
to the assignment of combination products because they explain how

various categories of both combination and single entity products were

classified2 and assigned3 to an agency center at the time the documents were

developed. The ICAs constitute guidance that is not binding on the public or the

agency (§ 3.5(a)(2)). The

ICAs are available at http://

www.fda.gov/oc/combination/

intercenter.html.

The agency has reviewed the ICAs and preliminarily determined that they

are generally consistent with the

requirements of section 503(g) of the act in that the principles used to assign

combination products described in the

ICAs are based on a product’s PMOA.

The ICAs were developed following the enactment of the statutory PMOA

criterion used to assign combination

products to an agency center, and were
developed using the PMOA principle.

For example, the CBER–CDRH ICA

assigns to CDRH products such as a

device incorporating a drug component

with the combination product having the primary intended purpose of

fulfilling a device function.” The

premise underlying the assignment to

CDRH is that the device component of

such a product provides the most

important therapeutic action of the

product. This ICA assigns to CDER

prefilled delivery systems, such as a

device with primary purpose of

delivering or aiding in the delivery of a

drug and distributed containing a drug.”

The premise of this assignment to CDER

is that the device’s primary purpose in
delivering or aiding in the delivery of a

drug is subordinate to the most

important therapeutic action provided by the drug product.

Similarly, the CBER–CDER ICA

assigns to CDER “combination products

that consist of a biological component

and a drug component where the

biological component enhances the

efficacy or ameliorates the toxicity of

the drug product.” The premise

underlying this assignment is that the

drug product provides the most

important therapeutic action of the

product, while the biological product

has a subordinate role in enhancing

such action.

FDA recognizes that, since the ICAs were written in 1991, new products

have been developed, new uses for existing products have been devised, and

additional laws, regulations, and guidelines are in effect. During this

period, FDA has continued to classify and assign many new products not

specifically covered by the ICAs. In

addition, some jurisdictional decisions made since 1991 cover products that

appear to be part of a broad class of product included in an ICA, but

are classified and/or assigned in a way different from the class of product

because of the particular product’s

specific characteristics or use. Many

of these decisions have been made through

the formal Request for Designation

(RFD) process. For these reasons, the

body of jurisdictional decisions has
grown over time, and the ICAs have

become incomplete statements. Moreover, in 2003 the agency

administratively transferred many

therapeutic biological products from

CBER to CDER. For this reason, the

CBER–CDER ICA is out of date.

IV. Preliminary Proposal to Continue in

Effect the CDER–CDRH and CBER–

CDRH ICAs, and to Rescind the CBER–

CDER ICA

The agency believes it is very

important to provide transparency in

jurisdictional decisionmaking. Such

transparency ensures predictability and

consistency of decisions, and decreases

ambiguity and uncertainty about agency

perspectives. Moreover, as the bases for

agency decisionmaking become clearer,

the need for formal RFDs and informal

inquiries covering specific products

may diminish, which should conserve

resources for the industry and the

agency.

A. CDER–CDRH and CBER–CDRH ICAs

The agency has reviewed the CDER–

CDRH and CBER–CDRH ICAs and

preliminarily determined that they

continue to provide helpful nonbinding

guidance, and so proposes to continue

them in effect, with the understanding

that they should not be independently

relied upon as the most current,

complete jurisdictional statements.

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2 Classification refers to the determination of a

product’s regulatory identity as a drug, device,

biological product, or combination product.

3 Assignment refers to the determination of the

agency center that will have primary jurisdiction for

the review and regulation of a product.
The agency considered updating the CDER–CDRH and CBER–CDRH ICAs as a way to continue to provide transparency to its jurisdictional decisionmaking. After consideration, however, the agency believes that the goal of transparency can be achieved more effectively by other means. The process of updating the ICAs would be time consuming, and given the quick pace of product development, the updated ICAs would soon be out of date as well. The agency believes that transparency is better served by articulating the principles upon which it bases determinations of a combination product’s PMOA, and by frequently issuing jurisdictional information on particular classes of products as that information becomes available. The agency suggests that persons wishing to get the most current information about jurisdictional determinations consult the numerous other sources of information about jurisdictional determinations described in this document, as well as the ICAs.

B. CBER–CDRH ICA

The 2003 administrative transfer of many therapeutic biological products from CBER to CDER has rendered the CBER–CDRH ICA out of date. For this reason, the agency preliminarily proposes to rescind the CBER–CDER ICA. A statement of the current assignment of biological products to CBER and CDER is available at http://www.fda.gov/oc/combination/transfer.html.

V. Actions Taken to Increase Transparency of Jurisdictional Decisionmaking

Since the enactment of MDUFMA, the agency has implemented, or is developing, the following actions to increase the transparency of jurisdictional decisionmaking:

A. Regulatory Definition of PMOA

As described previously in this document, the agency recently published a final rule defining “primary mode of action,” which is the basis for assigning a combination product to a lead center for review. The regulation includes an algorithm that will be followed when the most important therapeutic action of a combination product cannot be determined with reasonable certainty. This clarification of the PMOA principle is expected to significantly increase the transparency of the decision. One goal of the agency’s assignment of combination products to an agency center.

B. Guidance for Industry and FDA Staff: How to Write a Request for Designation (RFD)

The goal of the guidance is to provide recommendations regarding the type of information a sponsor should submit in order for the agency to determine the regulatory identity of a product as a drug, device, biological product, or combination product, and to assign the product to the appropriate agency component for review and regulation. The guidance reflects the final rule defining the PMOA of a combination product, and is expected to increase the transparency of the RFD process by clarifying the kind of information that enables the agency to make a prompt and appropriate assignment decision. The guidance is available at http://www.fda.gov/oc/combination/howtowrite.html.

C. Jurisdictional Determinations

The agency has made available on the OCP Web site more than 220 capsular descriptions of prior RFD decisions. In selecting which jurisdictional determinations were appropriate to summarize and make public in this way, the agency considered the extent to which the product could be suitably described, the extent to which the existence and description of the product or similarly described products have been made public, and related factors. The agency will continue to update the list of capsular descriptions as new decisions are made and as information on these products becomes publicly available. The capsular descriptions are available at http://www.fda.gov/oc/combination/determinations.html.

D. Jurisdictional Updates

Jurisdictional updates are more detailed statements of the classification and assignment of various product classes. They reflect past agency decisions, and are not intended to be policy statements. Jurisdictional updates generally contain information about the basis for the assignment and classification decisions that have been made. The agency selects product classes to be the subject of jurisdictional updates based on the agency’s perception of the current level of interest in the jurisdictional issue, the extent to which the class of products can be clearly described, the extent to which the existence and description of the class of products has been made public, and related factors. Additional jurisdictional updates will be issued as appropriate. Jurisdictional updates are available at http://www.fda.gov/oc/combination/updates.html.

E. RFD Decision Letters

The agency posts on the OCP Web site RFD decision letters for products that have been approved or cleared. These letters have been redacted to remove trade secret and confidential commercial information in accordance with the Freedom of Information Act. It should be noted that, in some cases, products undergo changes in name, sponsor, design, or other key aspects following the agency’s issuance of an RFD decision. The agency will post RFD decision letters when it is certain that the covered product has been approved or cleared, but it should be recognized that the posting may be incomplete. Posting of these letters, which generally include the agency’s reasoning behind the RFD decision, is intended to provide additional transparency on the jurisdictional process. The letters are available at http://www.fda.gov/oc/combination/rfd.html.

F. Chemical Action

In the course of assigning combination products to an agency center, OCP must often determine whether a product is a combination product—a determination that may turn on whether a constituent part of the product is properly classified as a device. Section 201(h) of the act (21 U.S.C. 321(h)) states that a device cannot achieve its primary intended purposes through chemical action within or on the body of man, or be dependent on being metabolized to achieve its primary intended purposes. The agency plans to develop guidance and/or regulations to further clarify what is meant by “chemical action” within or on the body. When final, such guidance and/or regulations should be helpful to sponsors in determining whether a product is a combination product.

G. Devices Regulated by CBER

Certain single entity (i.e., noncombination) devices are regulated under the device provisions of the act by CBER, rather than CDRH. One of the main purposes of the CBER–CDRH ICA is to identify categories of devices regulated by CBER. The agency believes, however, that additional guidance describing the assignment of devices that process human cellular and tissue products would be helpful. This product area was not fully envisioned at the time the CBER–CDRH ICA was developed. The agency plans to develop such guidance to assist sponsors in determining whether certain devices would be regulated by CDRH or CBER.
H. Combination Product Regulation

For some types of combination products, the CDER–CDRH ICA addresses good manufacturing practices, registration and listing, labeling, and other product regulation issues. The agency is developing guidance and/or regulations to address these and other significant areas of combination product regulation, and when final, these documents will ultimately update the limited information provided in the CDER–CDRH ICA on these topics.

VI. Practices Specific to Assignment of Combination Products

The agency has reviewed its practices specific to the assignment of combination products to ensure that they are in compliance with the requirement of section 503(g)(4)(B) of the act that the agency promptly assign a combination product to an agency center with primary jurisdiction in accordance with section 503(g)(1) of the act.

The agency has refined its processing of jurisdictional requests to ensure that the agency makes its assignments promptly. For example, section 503(g)(4)(A) of the act requires OCP, in determining whether a product is appropriately classified as a combination product, to consult with the component within the Office of the Commissioner that is responsible for such determinations. In the Federal Register of June 23, 2003 (68 FR 37075), the agency issued a final rule announcing that to enhance the efficiency of agency operations, OCP assumed responsibility from the Office of the Ombudsman for designating the component of FDA with primary jurisdiction for the premarket review and regulation of any product requiring a jurisdictional determination under part 3 (21 CFR part 3). This change consolidated the jurisdiction program within OCP, eliminated the requirement for consultation about the classification of a product as a combination product, and made the RFD program more efficient to administer. The final rule also provided for the electronic submission of RFDs (§ 3.7(d)).

Similarly, OCP has refined its internal processes and practices to ensure that all RFDs are resolved within the 60-day timeframe requirement of section 503(b)(1) of the act (21 U.S.C. 360bb–2(b)) (§ 3.8(b)). All RFDs submitted to OCP since its inception have been resolved within the 60-day period. Furthermore, all requests for reconsideration were responded to within the 15-day timeframe (§ 3.8(c)). For the period from the establishment of OCP through March 31, 2006, FDA’s average RFD processing time for assignments of combination products is 37.7 days (median 40 days, range 11–59 days). Accordingly, the agency has preliminarily determined that its practices are consistent with the requirement contained in section 503(g)(4)(B) of the act that it promptly assign combination products to an agency center based on the product’s PMOA. FDA plans to continue in effect the process improvements needed to maintain the prompt assignment of combination products, and plans to continue to work to refine its processes further.

VII. Comments

Interested persons may submit to the Division of Dockets Management (see ADDRESSES) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.


Jeffrey Shuren,
Assistant Commissioner for Policy.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, HHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7057; fax: 301/402–0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Mammalian Cell Surface Display of Fvs for Rapid Antibody Maturation

Description of Technology: This technology describes a new method of cell surface display of single chain antibodies for affinity maturation in a mammalian system. Cells expressing a rare mutant antibody with higher affinity were enriched about 240 fold by a single-pass cell sorting from a large excess of cells expressing wild-type antibodies with slightly lower affinity. Additionally, a highly enriched mutant with increased binding affinity for CD22 after a single selection of a combinatorial library randomizing an intrinsic antibody hotspot was successfully obtained. The system is compatible with other mammalian expression systems and it is a rapid, simple and robust procedure. The method can be useful in isolating high affinity antibodies for cancer, AIDS and other diseases.

Applications: (1) A new method of displaying Fvs on human cells; (2) A new method useful to isolate new high affinity antibodies for cancer, AIDS and other diseases.

Market: The method has a potential several billion dollar market as it can be potentially used in immunotherapeutic approaches for the treatment of cancer, AIDS and other diseases.

Development Status: The technology is currently in pre-clinical stage of development.

Inventors: Drs. Ira Pastan and Mitchell Ho (NCI).


Licensing Status: Available for non-exclusive or exclusive licensing.

Licensing Contact: Jesse S. Kindra, J.D.; 301/435–5559; kindra@mail.nih.gov.

Collaborative Research Opportunity: The National Cancer Institute Laboratory of Molecular Biology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize Mammalian Cell Surface Display of Fvs...