LOG OF MEETING

SUBJECT: Clinical Trial Packaging

DATE OF MEETING: August 18, 1999

PERSON SUBMITTING LOG: Laura E.W. Noble, *Chemicals, Clothing, and Household Products Team*, Office of Compliance

LOCATION: CPSC Headquarters, Bethesda, MD

CPSC ATTENDEE(S): See attached

NON-CPSC ATTENDEE(S): See attached

SUMMARY OF MEETING:

This meeting was requested by the Clinical Interest Group representatives. This meeting continued the dialog with the CPSC staff from our last meeting (May 18, 1999) and sought clarification of a letter, dated June 21, 1999, sent by the CPSC staff to the Clinic Interest Group. The June 21, 1999 letter detailed several options for which Compliance will exercise its enforcement discretion regarding the packaging of clinical trial drugs. A copy of that letter is attached.

A brief discussion was held regarding the historical perspective of clinical trials packaging.

The agenda for this meeting included discussion of the following issues:

- Rationale for decision to not include Phase IV studies in clinical packaging options
- Timeline for compliance with regulations affecting clinical packaging
- Clarification on labeling as it pertains to the clinical packaging options
- Opportunities/situations for a CR Waiver Statement in the Informed Consent Document
- Data from CPSC related to child poisonings related to investigational packaging access
- Acceptable size limits for Secondary CR packaging

The Clinical Interest Group committed to provide a letter to CPSC in the next few months in which the industry will detail specific issues for formal resolution by CPSC staff. Some of these specific issues include inclusion of Phase IV studies in the Compliance discretion for clinical trials packaging, and time frame for expected compliance for clinical trials packaging for current trials and trials not yet begun.

The staff will consider the Clinical Interest Group's letter when it is received.

Meeting with *Clinical Interest Group* representatives

Room 715, 10:00 a.m., August 18, 1999

ATTENDEES

Name	Company	Telephone Number
Laura Noble	CPSC-Compliance	301-504-0400 x1452
SUZANNE BARONE	CPSC - HS	301-504-0477 x 1196
JEWABE ASEBE	CPSC- EHHS	(301) 504-0477, Ext. 1379
TERRI Rogers	CPSC -Compliance	(301) 504-0608, ext 1363
Rick Schill	IMDG	(919) 483 - 4118
Edward Suez	EPICS	(610) 889-8774
Mike Dragoon	ISPE- Clinical Material Committee	607-335-6849
Frank J. Tiano	DIA - Contract Packaging	(215) 501-1201
Peter Mayberry	Healthcare Compliance Packaging Council	703/847-6727
GISELE CLOUTIER	HCPC	(703) 847-6727
Mike Gidding	CPSC/Compliance	301 504 0626 x1344
by Phone Chuck Carney	IMDG/ISPE	203-798-5259
Lori Padkul	MCSG	317-277--7436
Mike McNear		610-871-8423

CPSA 6 (b)(1) Cleared
X 6/24/99
No Mfrs/PrvtLblrs or Products Identified
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___Firms Notified,
Comments Processed.

U.S. CONSUMER PRODUCT SAFETY COMMISSION
4330 EAST-WEST HIGHWAY
BETHESDA, MD 20814

OFFICE OF COMPLIANCE
Chemicals, Clothing, and Household Products Team
Fax: 301-504-0359

Laura E.W. Noble
Compliance Officer
Tel: 301-504-0400, ext. 1452
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JUN 21 1999

Frank Tiano
PCI Services
3001 Red Lion Road
Philadelphia, PA 19114-1123

RE: Child-Resistant Packaging for Clinical Trials

Dear Mr. Tiano:

I am writing to follow-up on the May 18, 1999, meeting of the representatives from the Clinical Interest Groups with the U.S. Consumer Product Safety Commission (CPSC) staff. The staff appreciates the time the group spent explaining the clinical trial process.

We understand that your primary concern is the use of child-resistant packaging during phase III clinical trials which may require the use of unit packaging due to the complexity of the studies and the importance of the compliance aspects of these types of trials. This packaging is specialized for these trials and may not necessarily be used when the product is marketed. During our meeting, you expressed concern that the development of "child-resistant" unit packaging is difficult as well as time and cost prohibitive because of the varying amounts and types of drugs used during cross-over and titration studies.

The CPSC staff appreciates the need to ensure patient compliance during clinical trials. However, we do have concerns about patients bringing drugs into the household that are toxic and in non-child-resistant packaging. As we informed you, it is the Commission's position that all prescription drugs for human use intended for oral administration must comply with the child-resistant packaging requirements unless specifically exempted in 16 C.F.R. § 1700.14.(a)(10). Additionally, over-the-counter drugs used in clinical trials that are dispensed for out-patient use must comply with the child-resistant packaging requirements if they are subject to one or more of the regulations issued under the PPPA.

The CPSC staff has discussed the issues involving child-resistant packaging of clinical trial drugs and offers the following guidance about drug packaging for phase II and III clinical trials. It should be noted that these compliance policies are restricted to phase II and III clinical trial drug packaging. These recommendations are **not** for usage for approved prescription drugs, including those used during phase IV clinical trials.

During phase II or III clinical trials:

Non-child-resistant packaging may be used if the amount of drug that is dispensed into the household will not cause serious injury or illness to a young child. (For example, the drug is of low toxicity or the amount of drug sent home is restricted to a level that is of low toxicity). Companies packaging clinical trial drugs who wish to take advantage of this option must maintain data that demonstrate that the product would not be expected to cause serious injury to children. This data will be made available to CPSC staff upon request.

Clinical trial drugs with sufficient toxicity to cause serious injury or illness to a young child must be packaged with a child-resistant feature. This can be achieved in one of two ways. The units can be made with any of the features described in ASTM D-3475, provided that the unit dose packaging has at least one recognized child-resistant feature. Alternatively, non-child-resistant units can be placed in an outer container that meets the standards of 16 C.F.R. § 1700.15.

It is noted that these options are not normally available under the PPPA. However, because of the unique situation presented by phase II and phase III clinical trials (i.e., individual packaging, patient compliance, etc.), we will exercise our enforcement discretion with regard to phase II and phase III clinical trials packaging.

This determination is based solely on the information currently available to the staff and the enforcement posture the CPSC currently has in effect. It could be changed if the facts change, and could be changed or superseded by the Commission.

If you have questions about the subject of this letter, please feel free to write or call me.

Sincerely,

Laura E.W. Noble

Laura E.W. Noble
Compliance Officer

cc: Dr. Lumpkin, FDA

Clinical Services MEMORANDUM

TO: Laura Noble, Consumer Product Safety Commission

FROM: Anne McGrogan

DATE: September 24, 1999

SUBJECT: Meeting Notes – 8/18/99

CPSA 6 (b)(1) Cleared
10/4/99
No Mfrs/PrvtLblrs or Products Identified
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Dear Laura,

Enclosed is the final on the notes from your meeting with Frank Tiano and group. Your changes were incorporated into the document. Please add this summary to the meeting log notes.

Thank you and if you have any questions, please don't hesitate to contact me.

Regards,

Anne McGrogan

Anne McGrogan

PCI CLINICAL SERVICES

Consumer Product Safety Commission (CPSC)
Meeting with Clinical Interest Group Representatives
8/18/99

Attendees:

CPSC
Suzanne Barone, Project Manager - Poison Prevention
Mike Gidding, Compliance Attorney
Laura Noble, PPPA Compliance Officer
Tewabe Asebe, Packaging Engineer
Terri Rogers, Acting Associate Director - Recalls and Compliance

Clinical Materials Interest Groups
Mike Dragoon, Clinical Materials Committee, ISPE, International Society for Pharmaceutical Engineering
Rick Schill, IMDG, Investigational Materials Discussion Group
Ed Suez, EPICS, Equal Partners in Clinical Studies
Frank Tiano, CSG, DIA & Contract Packaging, Clinical Supplies Group
Via Phone:
Chuck Carney, ISPE, International Society for Pharmaceutical Engineering
Mike McNear, CCP, Clinical Contract Packaging
Lori Podkul, MCSG, Midwest Clinical Supply Group

Healthcare Compliance Packaging Council (observers only)
Peter Mayberry
Gisele Cloutier

Clinical Interest Groups

- Clinical Contract Packagers (CCP) – Mike McNear
- Clinical Materials Committee (CMC) of ISPE – Mike Dragoon, Chuck Carney
- Clinical Studies Support Group (CSSG) – Marty Jeiven
- Clinical Supplies Group (CSG) of DIA – Frank Tiano
- Equal Partners in Clinical Studies (EPICS) – Ed Suez
- Investigational Materials Discussion Group (IMDG) – Rick Schill
- Midwest Clinical Supply Group (MCSG) – Lori Podkul
- Pacific Area Regional Clinical Supply Group (PARCS) David Bernstein

This summarizes key points from the second meeting on Child Resistant Packaging use in clinical trials. The two parties involved were the Consumer Product Safety Commission (CPSC) and representatives from various Clinical Interest Groups throughout the United States. The purpose of the meeting was to clarify several points from the June 21, 1999 letter re: Child-Resistant Packaging for Clinical Trials from Laura E. W. Noble, Compliance Officer, CPSC.

1. Phase IV exemption from CPSC recommendations on compliance policies in 6/21/99 letter.

    - The Clinical Material Interest groups clarified that the special challenges faced in phase II and phase III trials are identical to the challenges faced in phase IV trials regarding the need for blisters. Simply because the products used in phase IV trials are marketed products does not mean that the products will be used in their marketed packages. In many cases, the product will be manipulated e.g overencapsulation, and repackaged into a blister card presentation.
    - CPSC understood this and will consider categorizing Phase IV trial supplies with Phases II and III when it is not possible to use the commercially available package.
    - When commercially available product is used in a study in an unblinded state (i.e. rescue medication), a commitment was made to offer the CR market presentation.

2. Timeline for Compliance

    - The CPSC suggested we draft a letter to them stating the specific concerns or issues with literal interpretation (i.e. applies today), along with rationale and proposals for addressing a phase in period for implementation. They stated that, pending their judgment on the merits of the proposal, they could take it up for compliance review and consideration.
    - The difficulty for implementation of CR in ongoing studies was presented. This will be addressed in the draft letter.

3. Clarification on labeling with respect to clinical packaging options

   - CPSC indicated that no special labeling statements are required if CR packaging is used.
   - A company may voluntarily include statements to alert patients to the presence or absence of the CR features(s).
   - Use of a non-CR statement on the primary non-CR package is advisable when used in conjunction with a CR secondary package.

4. Opportunities/Situations for a CR Waiver Statement in the Informed Consent Document.

   - This option, which was discussed in our 5/18/99 meeting, was not mentioned in the CPSC 6/21/99 letter. Clinical Material Group individuals noted this absence and brought it to the attention of CPSC.
   - According to CPSC, the options available to us must incorporate physician involvement in assessing dispensation of drug to individual patients. A "blanket" waiver, with due consideration to CR packaging unavailability is not appropriate, per CPSC.
   - CPSC pointed to use of physician discretion on a case by case basis after assessment of patients' special needs.
   - CPSC did indicate that they would take a dim view of a physician who dispensed non-CR packaging to homes with young children.
   - CPSC will frown on non-CR packaging used in a study base with the hope that the investigator will hand out the clinical trial materials.
   - A study should include the option for CR packaging.
   - Application or removal of a secondary CR package would present the option of providing both CR and non CR supplies.
   - A waiver statement would be at the discretion of the pharmaceutical company and not mandated by CPSC.

5. Data from CPSC related to child poisonings related to clinical packaging access.

   - Data regarding child poisonings related to clinical packaging access is anecdotal. (comments from hospital pharmacists)
   - Poison control centers do not have this information readily available due to the way clinical studies are conducted.
   - There were a small number of child access cases, involving clinical trial materials, according to CPSC.

- CPSC personnel indicated that if there were an "epidemic" of cases involving this matter, the CPSC would be taking a very different stance. They further indicated that they would utilize their enforcement discretion in this matter.

6. Secondary CR Packaging

- Testing of primary CR packaging is not necessary if the units can be made with any of the features described in ASTM D-3475, provided that the unit dose packaging has at least one recognized child-resistant feature. (Note: ASTM D-3475 is being revised at this time)
- CR packaging is not necessary if the non-child-resistant units can be placed in an outer container that meets the standards of 16 CFR 1700.15.
- The above exceptions were made only because of the unique situations presented by clinical trial supplies.
- Secondary CR packaging may be the only efficient method of offering an option to patients.
- CPSC preferred to see individual secondary package CR presentation rather than bulk secondary packs (i.e. carton containing multiple weeks worth of supplies).
- Larger size packaging with boxes, locks, keys, etc. would not be favorably viewed by CPSC.
- Concern was raised regarding the space that might be consumed by large secondary packages.
- CR pouches must be resealable (the CR feature reactivated) if the primary container holds more than a single dose.

Next Steps

1. Clinical Materials Interest Group will submit notes to CPSC (within 30 days).
2. CPSC will add this Meeting Notes Summary to the meeting log notes on file (requirement of CPSC).
3. Clinical Materials Interest Group representatives will review status with specific Clinical Material Interest Groups. Input will be gathered. (Meetings scheduled in October)
4. A draft letter to CPSC regarding a phase-in period proposal will be written by the interest groups. (January 2000)
5. CPSC will review and respond to the letter.