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Protein Adducts for Exposure Monitoring: A Computerized Database

Software and User's Manual

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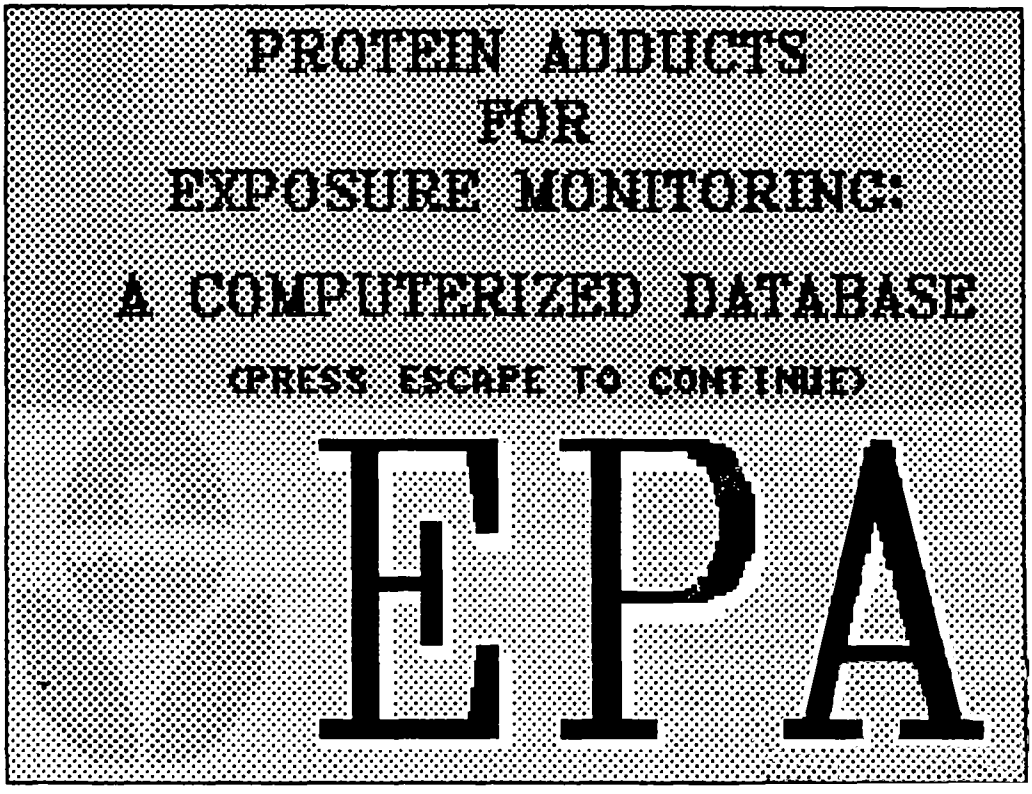

USER'S MANUAL TO EPA'S PROTEIN ADDUCTS DATABASE

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NOTICE

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ABSTRACT

The Computerized Protein Adducts Database (CPAD) was created to provide an efficient means of updating and disseminating information on protein adducts relating to their utility as dosimeters of exposure to environmental contaminants, especially genotoxic and/or carcinogenic compounds. The structure of the database as well as its initial contents were derived primarily from the document, "Protein Adduct-Forming Chemicals for Exposure Monitoring: Chemicals for Further Study" (EPA/600/4-89/035).

The programs that enable the user to search, modify, or update the database and display its contents were originally written in the DBASE III PLUS™ programming language, then converted, compiled and linked by DBASE IV™, version 1.1. The final product is a user-friendly, menu-driven, stand-alone DBASE application that requires little from the user beyond the ability to read the screen and operate a keyboard. Even a "User's Manual" is, to some extent, superfluous. The present document largely represents a "hard" copy of documentation that is already provided within the program itself. The CPAD diskette also contains a copy of this document which may be viewed on screen or printed out as a WORDPERFECT™ 5.0 document file .

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INTRODUCTION

PROJECT BACKGROUND

The Environmental Protection Agency (EPA) has executed its mandate to protect human health and the environment by placing restrictions and regulations on the use of chemicals that have been shown to be detrimental to human health or the environment. In addition, the Agency has developed an initiative designed to develop, refine and apply appropriate biomarkers for use in conjunction with environmental monitoring data to provide better estimates of exposure and risk to individuals and populations. Only by relating biological measurements to environmental monitoring measurements can the relationships between total exposure, effective dose and disease be determined.

In a 1987 report entitled "Carcinogen-DNA Adducts: Introduction, Literature Summary and Recommendations" (EPA/600/4-87/005), it was recognized that hemoglobin and serum albumin adducts may be more advantageous than DNA adducts as biological markers of exposure, because protein adducts are typically more stable and more abundant than DNA adducts. A subsequent report entitled "Protein Adduct-Forming Chemicals For Exposure Monitoring: Literature Summary and Recommendations" (EPA 600/4-90/007) summarized the literature regarding adducts formed by xenobiotics with proteins, particularly hemoglobin and serum albumin, and examined the feasibility of their use as dosimeters of exposure. Those chemicals of interest to the EPA that were recommended for further study were ranked according to their potential utility in exposure monitoring by protein adduct-based methods. These prioritized chemicals (22 in number) were examined in greater detail in a report entitled "Protein Adduct-Forming Chemicals For Exposure Monitoring: Chemicals Selected for Further Study" (EPA/600/4-89/035).

It was anticipated that, due to rapid developments in the field of molecular dosimetry, the information in the last-mentioned protein adducts report, as well as the prioritized chemicals list, itself, would require frequent amendments and updates in the future. To facilitate that process, the Computerized Protein Adducts Database (CPAD) was developed. The structure of the database as well as its initial contents were derived primarily from the above-mentioned document, "Protein Adduct-Forming Chemicals for Exposure Monitoring: Chemicals Selected for Further Study" (EPA/600/4-89/035). The database includes entries on the following topics: manufacture and use, sources and levels of exposure, known health effects, metabolism

(detoxification and activation), host factors, reactive metabolites, adduct characterization, rates of adduct formation (i.e., second order rate constants), background adduct levels, dose-response relationships, and methods of adduct detection.

INSTALLATION AND STARTUP OF CPAD

THE DBASE™ III PLUS VERSION

The database proper (i.e., SPADDUCTS.DBF) is a DBASE™ III PLUS file. So that users unfamiliar with DBASE™ would have ready access to the data in CPAD, some 32 program files were written in the DBASE™ III PLUS programming language, then compiled and linked into a single program file (PADDUCTS.PRG) to create a user-friendly, menu-driven DBASE™ application. (Note: in addition to PADDUCTS.PRG, this version requires thirteen accompanying *.FRM files in order to run.) This version of CPAD may be used with or without DBASE™ III PLUS.

IF YOUR COMPUTER DOES HAVE DBASE™ III PLUS INSTALLED, ONLY THE FILES IN THE CPAD.DB3 DIRECTORY OF THE 3.5" CPAD DISKETTE NEED BE COPIED TO A SEPARATE DATA SUBDIRECTORY ON YOUR HARD DRIVE (e.g., c:\CPAD). These files will require approximately 270K of memory on your hard disk. IF YOUR COMPUTER DOES NOT HAVE DBASE™ III PLUS INSTALLED, THEN THE THREE DBRUN FILES IN THE RUNTIME.DB3 DIRECTORY OF THE CPAD DISKETTE MUST ALSO BE COPIED INTO THE CPAD DIRECTORY ON YOUR HARD DISK. These files will run CPAD in exactly the same way that DBASE™ III PLUS would, but, unlike the DBASE™ system files, these DBRUN files can be legally copied and distributed along with the CPAD files.

Other directories on the CPAD diskette contain the source code (i.e., SRC files) and the object code (i.e., PRG files) that were used in conjunction with the DBASE™ III PLUS utilities dbc.com and dbl.com to generate the linked file padducts.prg. These files are not required to run CPAD and are included only for the information of users interested in the program's design.

THE DBASE™ IV, 1.1, VERSION

For the benefit of those who have DBASE™ IV, version 1.1, installed on their computers, a compatible version of CPAD has been included in the CPAD.411 directory of the CPAD diskette. In this version of CPAD, all program and report form files from the DBASE™ III PLUS version have been converted to DBASE™ IV version 1.1 format. The resulting files (44 in all) were then compiled and linked to form the single file, MAINMENU.DBO. (Note: The drivers IBMPRO_1.pr2 and PRNTFRM.PRF in the CPAD.411 directory are required for the operation of the DBASE™ IV version of CPAD, even though the printer itself, regardless of brand, is not used by the program.)

To install this version of CPAD, simply COPY ALL THE FILES FROM THE CPAD.411 DIRECTORY OF THE CPAD DISKETTE TO A SEPARATE SUBDIRECTORY ON YOUR HARD DRIVE (e.g., c:\CPAD). You will need only about 325K of disk space for the DBASE™ IV version, since no Runtime files are required. However, THIS VERSION OF CPAD ONLY WORKS IF DBASE™ IV, VERSION 1.1, IS INSTALLED ON YOUR COMPUTER. Your DBASE™ IV directory must also be in the path statement of your autoexec.bat file. A stand-alone (Runtime) DBASE™ IV, 1.1, version of CPAD is not included. The stand-alone (DBRUN) DBASE™ III PLUS application is the best choice for computers without DBASE™ installed because (1) it requires a million bytes less than would a DBASE™ IV, 1.1, Runtime version and (2) it runs better than the DBASE™ IV version which occasionally exibits some minor but irritating "quirks" during data entry.

The directories SRCCODE.411 and OBJCODE.411, respectively, contain source code (i.e., PGR and FRM files) and object code (i.e., DBO and FRO files). The 44 object files were combined into a single large file (Mainmenu.dbo) using the DBASE™ IV (version 1.1) utility DBLINK.EXE. (See Appendix D.)

GETTING STARTED

To run either version of CPAD, simply enter "START" from within the subdirectory that contains the CPAD files (and the three DBRUN files, in the stand-alone version). Alternatively, the compatible version of CPAD may be run from within DBASE™ III PLUS or DBASE™ IV by entering "DO PADDUCTS" or "DO MAINMENU", respectively, at the dot prompt, provided that (1) DBASE is loaded from within your CPAD directory, thereby making it the default directory, and (2) the DBASE directory is in your PATH statement. It would also be useful to write a batch file (e.g., CPAD.bat) that would allow you to load CPAD from the root directory.

The internal documentation of CPAD should prove sufficient for those users who like to jump right in and play with a new program. For those preferring a more structured approach, the material that follows is provided. It leads the reader step-by-step through all the screens of CPAD, briefly describes its various features and reiterates certain hints and warnings provided within the program, itself. All the illustrations in this manual, including those on the cover and back page, represent actual screens from CPAD. Any comments or questions about CPAD should be directed to Charles Nauman at the following address: United States Environmental Protection Agency, Environmental Monitoring Systems Laboratory, Exposure Assessment Research Division, P.O. Box 93478, Las Vegas, NV, 89193-3478.

SEARCHING THE DATABASE

THE MAIN MENU

Pressing ESCAPE at the TITLE SCREEN loads the program file PADDUCTS.PRG or MAINMENU.DBO, depending on the version of CPAD (i.e., DBASE™ III PLUS or DBASE™ IV, ver.1.1). The total number of records (i.e., chemicals) contained in the database is determined and displayed on THE MAIN MENU (Figure 1), along with the first seven chemicals in alphabetical order. As indicated by the prompts at the top and bottom of the screen, the rest of the alphabetical listing may be viewed in either of two ways:

1.) the user may scroll forward or backward a "page" at a time by pressing the PGDN or PGUP key, respectively, or

2.) if the user is searching for a specific chemical record, he may skip to the appropriate portion of the alphabetical listing by entering the first letter in the name of the chemical. (Note: any leading numerals or greek letters in the chemical name are placed at the end of the name so as not to interfere with the alphabetical sorting of records.)

Once the desired chemical record has been displayed on the screen by one or a combination of the above methods, that record is selected for viewing or editing by entering the corresponding number (up to 3 digits). (Note: In the DBASE™ IV version, an audible "beep" indicates the program is ready for user input.) The name of the selected chemical will appear on all subsequent screens. Other options available at the main menu are "Exit to DOS" (F10) and "ADD/DELETE RECORD".

THE DATA DISPLAY SCREENS

Immediately after a selection is made, the name of the selected chemical is displayed on THE MAIN FIELD-SELECTION MENU (Figure 2) along with the following options:

1.) View fields containing information on the selected chemical (enter 1),

2.) View fields containing information on protein adducts formed by the chemical (enter 2), and

3.) View all fields in sequence (enter 3).

Figure 1 **The Main Menu**

PGUP/PGDN = SCROLL F8 = ADD/DELETE RECORD 510 = EXIT TO DOS

(THERE ARE A TOTAL OF 22 RECORDS TO VIEW)

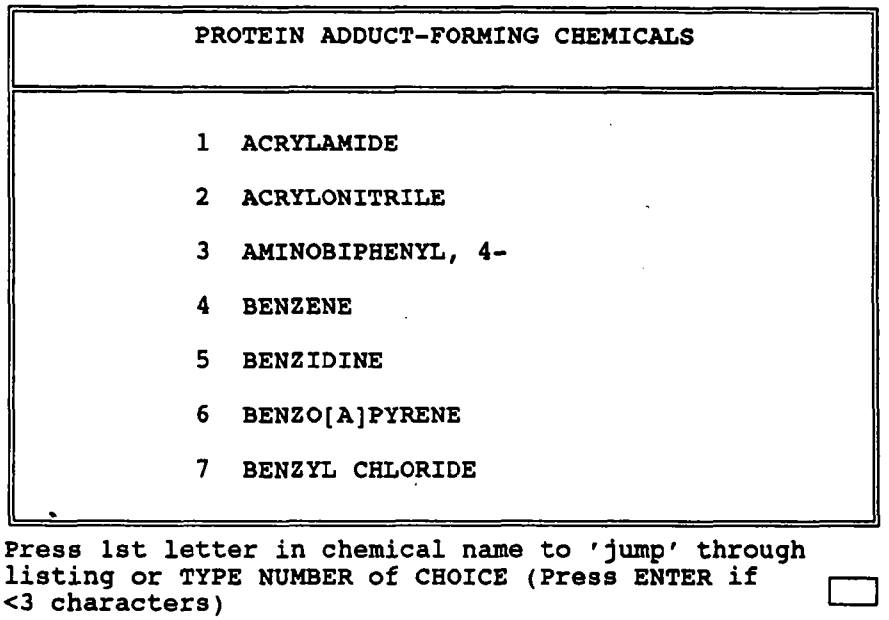
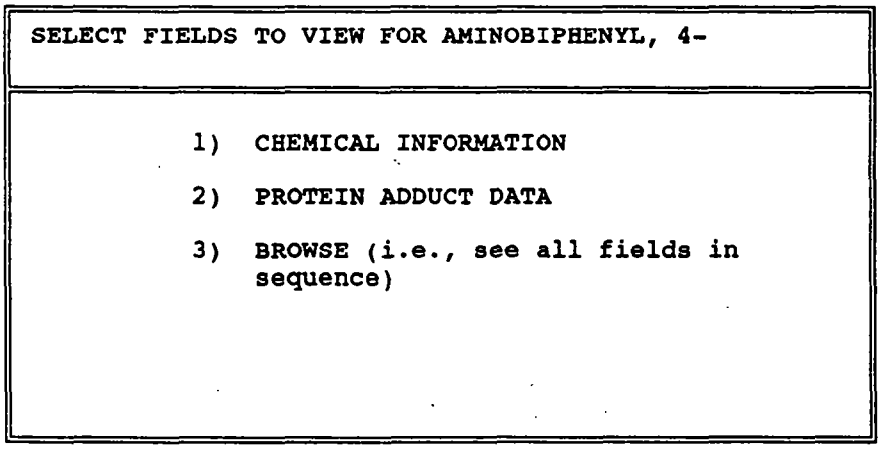


Figure 2 **The Main Field-Selection Menu**

(F9) PREVIOUS MENU (F10) QUIT



CHOOSE ONE

Other options available at this menu are: return to "PREVIOUS MENU" (F9) and "QUIT" (F10). Throughout the program, "Quit" and Exit to DOS" are synonymous.

CHEMICAL DATA SCREENS

Selecting 1 at the MAIN FIELD-SELECTION MENU will cause the CHEMICAL DATA FIELDS MENU (Figure 3) to be displayed on the screen. From this menu, one may select any of the following database fields to view: CAS NUMBER, SYNONYMS, volume and method of MANUFACTURE, major USES, sources and levels of EXPOSURE, HEALTH EFFECTS, METABOLISM (Detoxification and Activation) and HOST FACTORS relating to metabolism and susceptibility. A field is selected by entering the letter (A-I) to the right of the field name. The BROWSE option (I) allows the user to view all the chemical data fields in sequence. Other options available at the Chemical Fields Selection Menu are: return to the PREVIOUS MENU (F9) and QUIT (F10).

Entering a letter (A-I) at the CHEMICAL DATA FIELDS MENU causes one of the chemical data display screens (Figures 4-11) to appear on the screen, along with the prompt " AFTER VIEWING DATA, PRESS A FUNCTION KEY TO PROCEED". The function keys referred to are those defined at the top of the screen, i.e., F8, F9 and F10. If you wish to modify the data displayed on the screen, select F8 (EDIT SCREEN). If you wish to exit to DOS, press F10 (QUIT). Pressing F9, the CONTINUE option, has two different effects, depending upon what was selected at the CHEMICAL DATA FIELDS MENU. If you choose the BROWSE mode (I), then pressing F9 will produce the next data display screen in the sequence. If you selected a specific data display screen (A-H), then pressing F9 will return you to the CHEMICAL DATA FIELDS MENU where you can make another selection, return to earlier menus or exit to DOS.

Note that the MANUFACTURE, EXPOSURE and METABOLISM screens (Figures 6, 8 and 10, respectively) each display two fields rather than one as the others do. Although the SYNONYMS screen (Figure 5) displays up to six different synonyms for the selected chemical name, all the synonyms for a chemical are stored in a single field and separated by semicolons. As discussed in the next chapter, "Modifying the Database", this fact becomes important when editing data in the synonyms field.

PROTEIN ADDUCT DATA SCREENS

Selecting 2 at the MAIN FIELD-SELECTION MENU will cause the PROTEIN ADDUCT FIELDS MENU (Figure 12) to be displayed on the screen. From this menu, which operates the same way that the CHEMICAL DATA FIELDS MENU does, one may select any of the following database fields to view: REACTIVE METABOLITES, (protein) ADDUCTS FORMED, (*in vivo* second order) RATE CONSTANT,

Figure 3 **The Chemical Data Fields Menu**

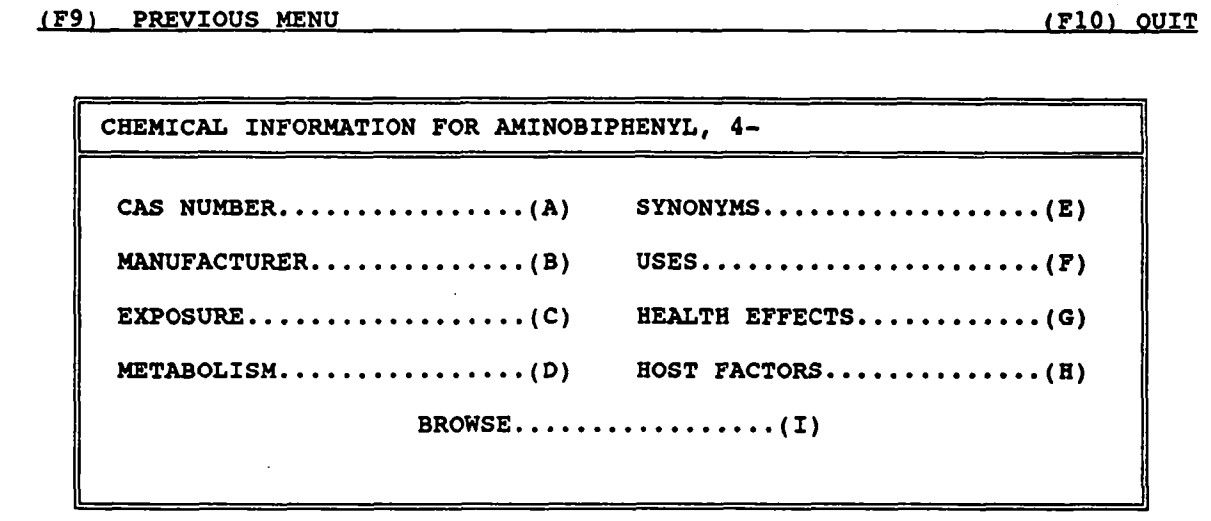


Figure 4 **The CAS Number Screen**

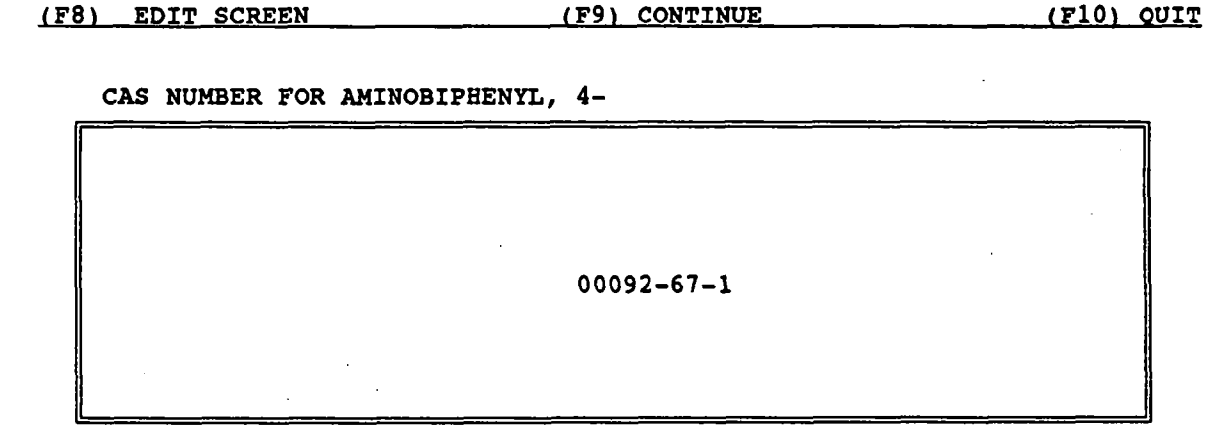


Figure 5 **The Synonym Screen**

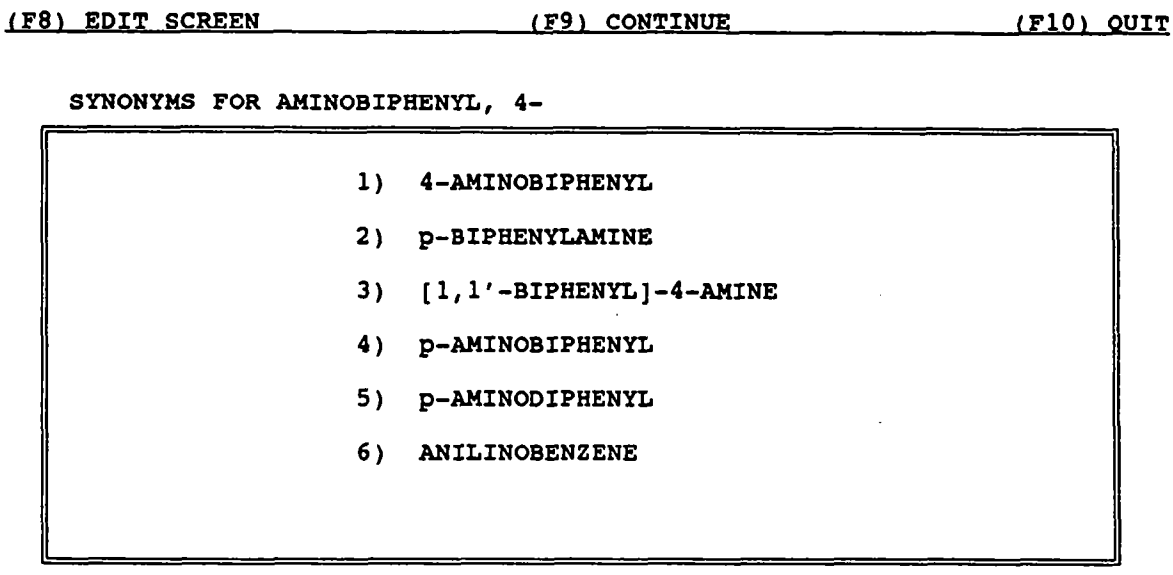


Figure 6 **The Manufacturing Data Screen**

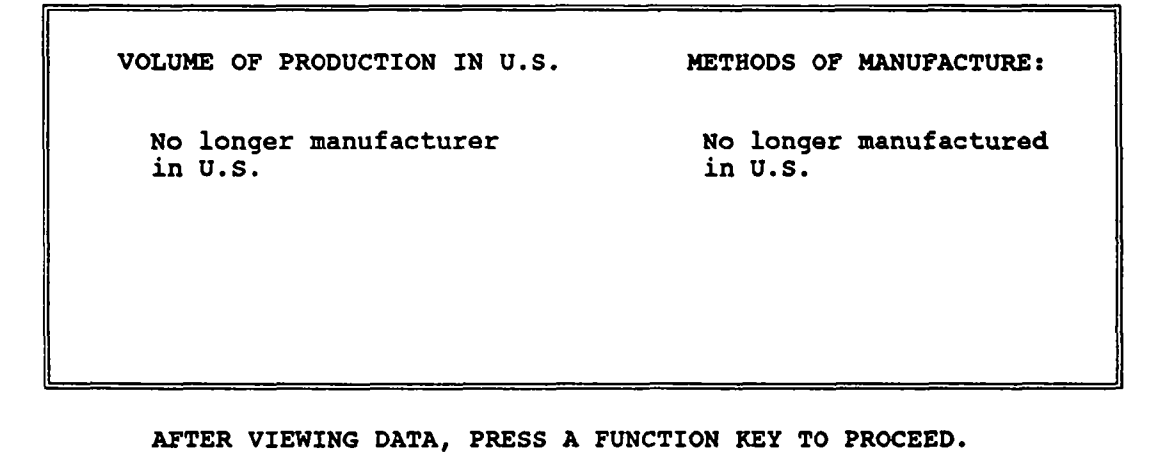


Figure 7 **The Major Uses Screen**

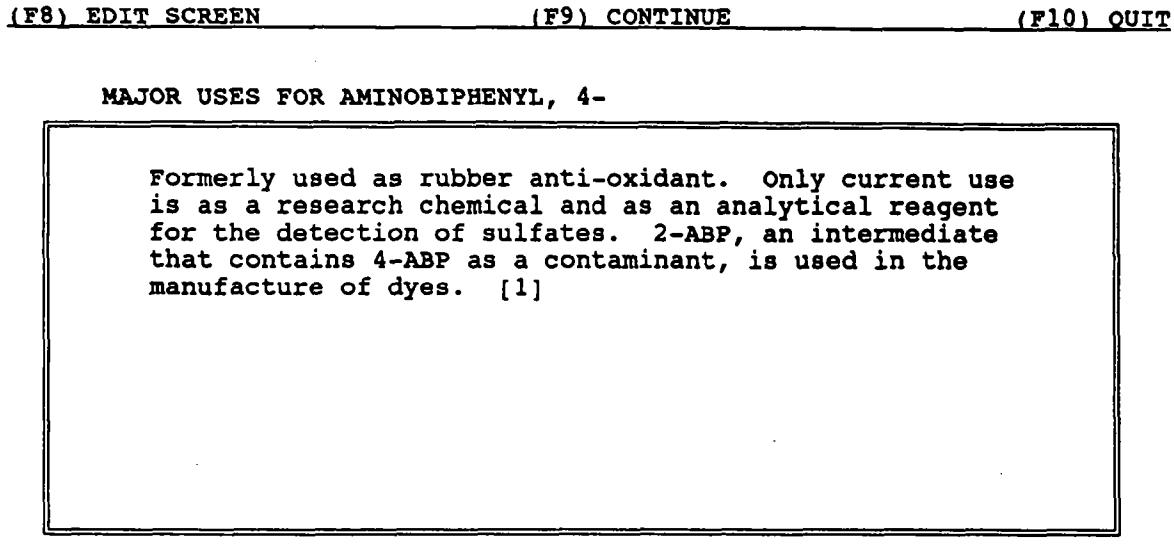


Figure 8 **The Exposure Data Screen**

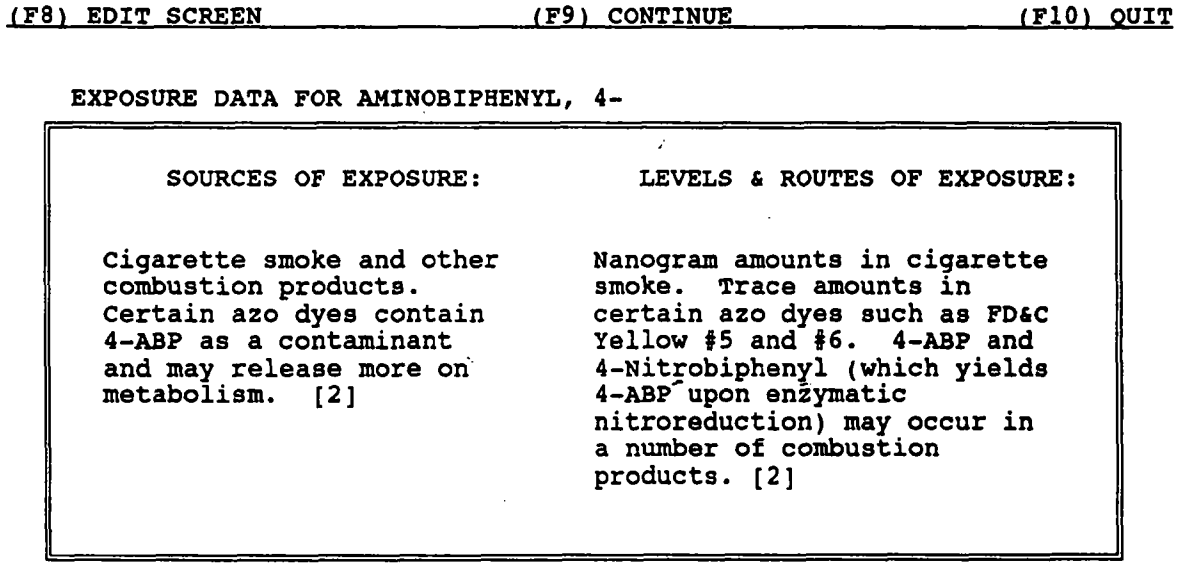


Figure 9 **The Health Effects Screen**

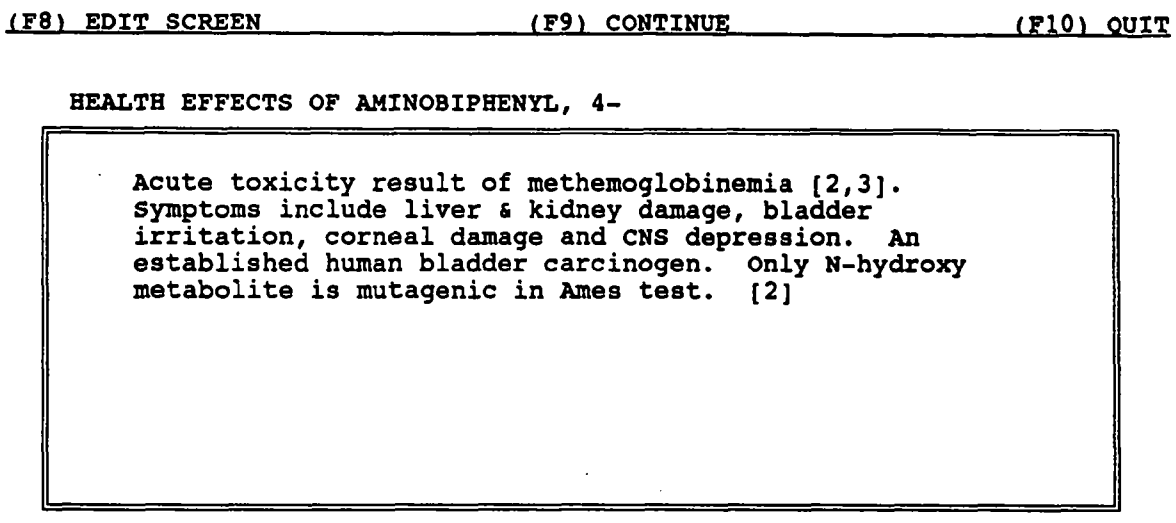


Figure 10 **The Metabolism Data Screen**

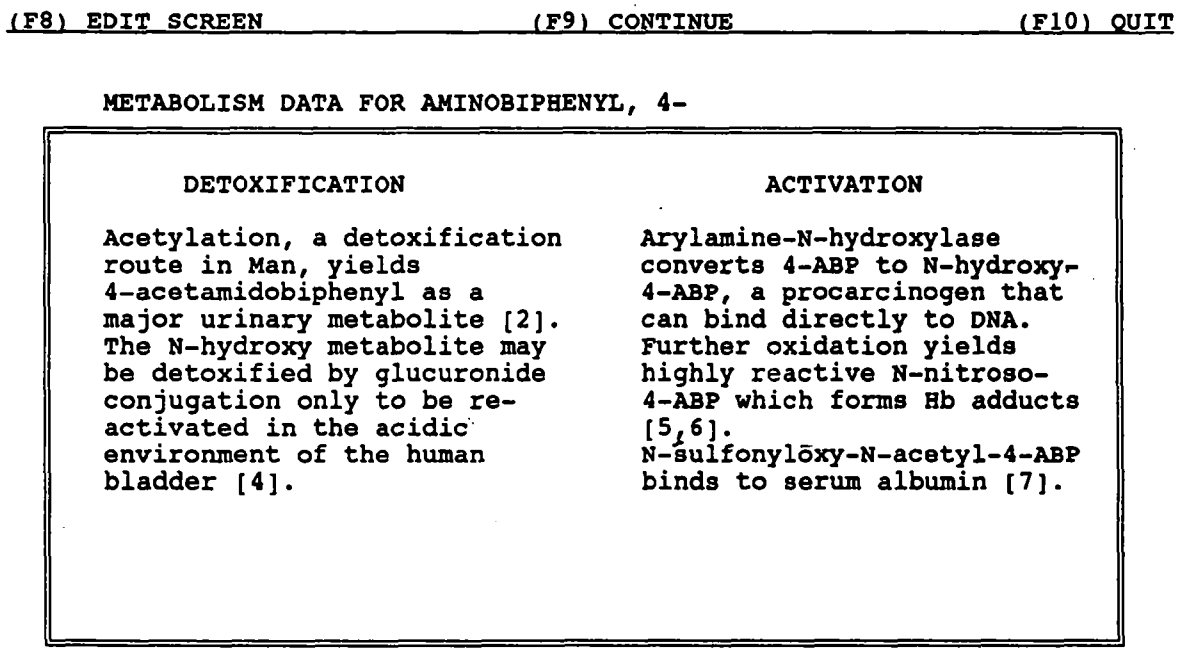


Figure 11 **The Host Factors Screen**

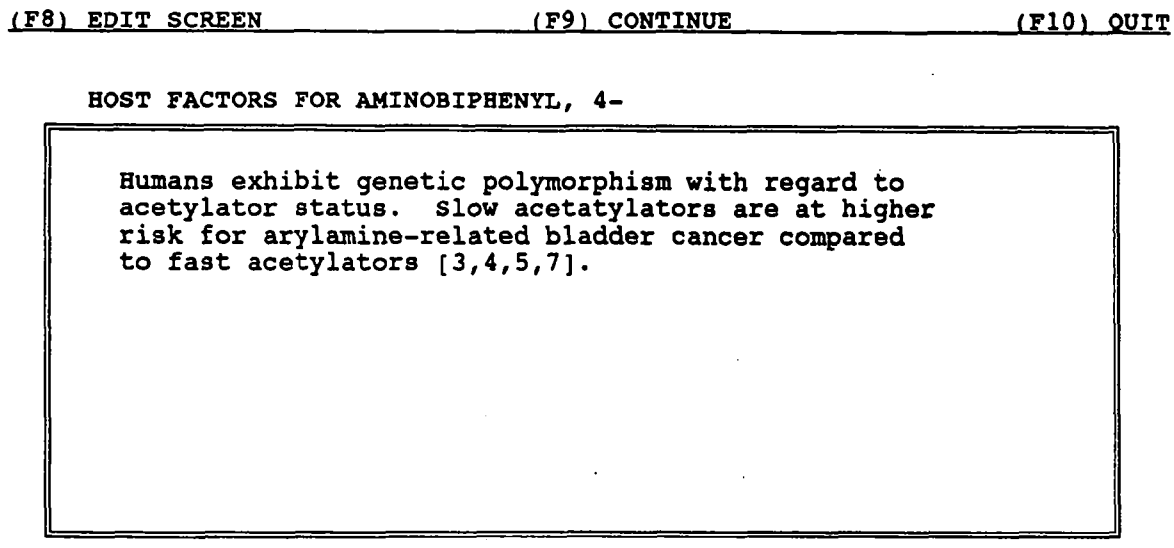
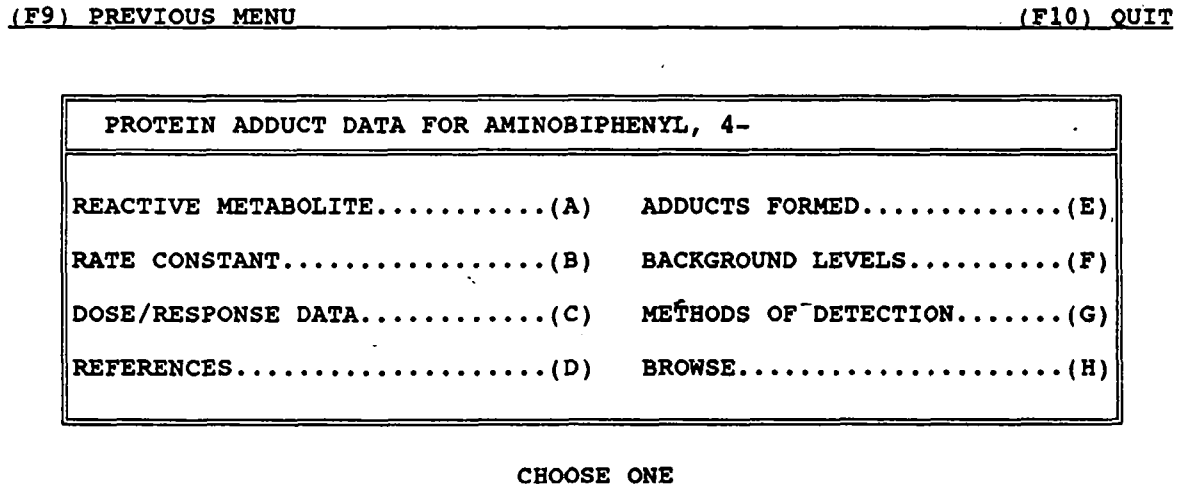


Figure 12 **The Protein Adduct Fields Menu**



BACKGROUND LEVELS (of adducts), DOSE/RESPONSE DATA, METHODS OF (adduct) DETECTION and REFERENCES. A field is selected by entering the letter (A-H) to the right of the field name. The BROWSE option (H) allows the user to view all the protein adduct data fields in sequence. Other options available at the PROTEIN ADDUCT FIELDS MENU are: return to the PREVIOUS MENU (F9) and QUIT (F10).

Entering a letter (A-H) at the PROTEIN ADDUCT FIELDS MENU causes one of the protein adduct data display screens (Figures 13-19) to appear on the screen, along with the prompt "AFTER VIEWING DATA, PRESS A FUNCTION KEY TO PROCEED". The function keys referred to are those defined at the top of the screen, i.e., F8, F9 and F10. If you wish to modify the data displayed on the screen, select F8 (EDIT SCREEN). If you wish to exit to DOS, press F10 (QUIT). As in the CHEMICAL DATA FIELDS MENU, pressing F9, the CONTINUE option, has two different effects, depending upon what was selected at the PROTEIN ADDUCT FIELDS MENU. If you choose the BROWSE mode (H), then pressing F9 will produce the next data display screen in the sequence. If you selected a specific data display screen (A-G), then pressing F9 will return you to the PROTEIN ADDUCT FIELDS MENU where you can make another selection, return to earlier menus or exit to DOS (i.e., Quit).

Note that, with the exception of the REFERENCES screen (Figure 19), all of the protein adduct data display screens are single-field displays. The REFERENCES screen, unlike the SYNONYMS screen (Figure 5), displays seven separate fields, one for each of a maximum of seven citations.

Figure 13 **The Reactive Metabolites Screen**

(F8) EDIT SCREEN (F9) CONTINUE (F10) QUIT

REACTIVE METABOLITES OF AMINOBIPHENYL, 4-

N-Hydroxy-4-ABP, co-oxidized to the nitroso cmpd. by heme, forms sulfinamide adducts at the beta-93 cysteine of Hb [5]. N-Sulfonyloxy-acetyl-4-ABP forms a unique tryptophan adduct with serum albumin [7].

AFTER VIEWING DATA, PRESS A FUNCTION KEY TO PROCEED.

Figure 14 **The <u>in Vitro</u> Rate Constant Screen**

(F8) EDIT SCREEN (F9) CONTINUE (F10) QUIT

IN VITRO RATE CONSTANT FOR AMINOBIPHENYL, 4-

Specific value unavailable as of 5-22-90.

AFTER VIEWING DATA, PRESS A FUNCTION KEY TO PROCEED.

Figure 15 **The Major Adducts Screen**

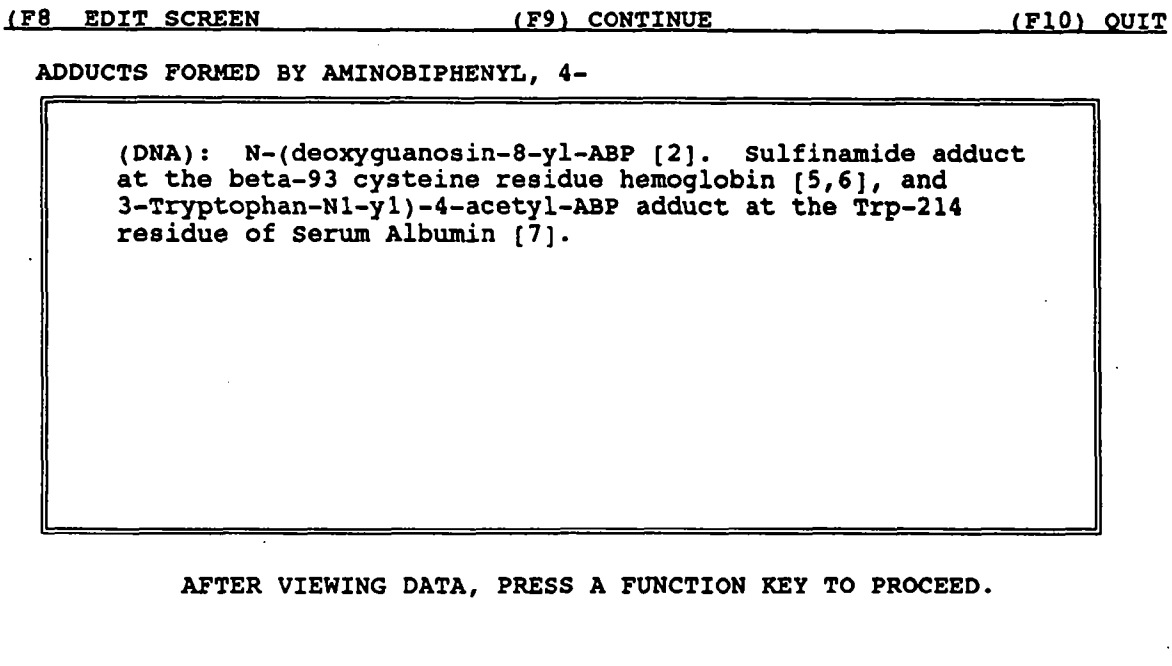


Figure 16 **The Background Adduct Levels Screen**

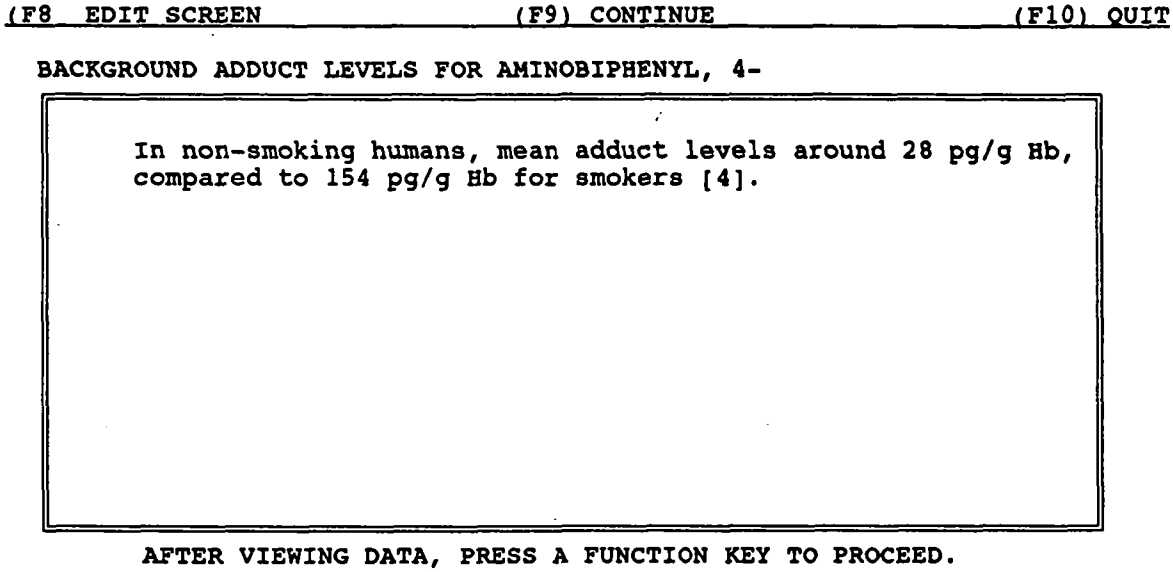
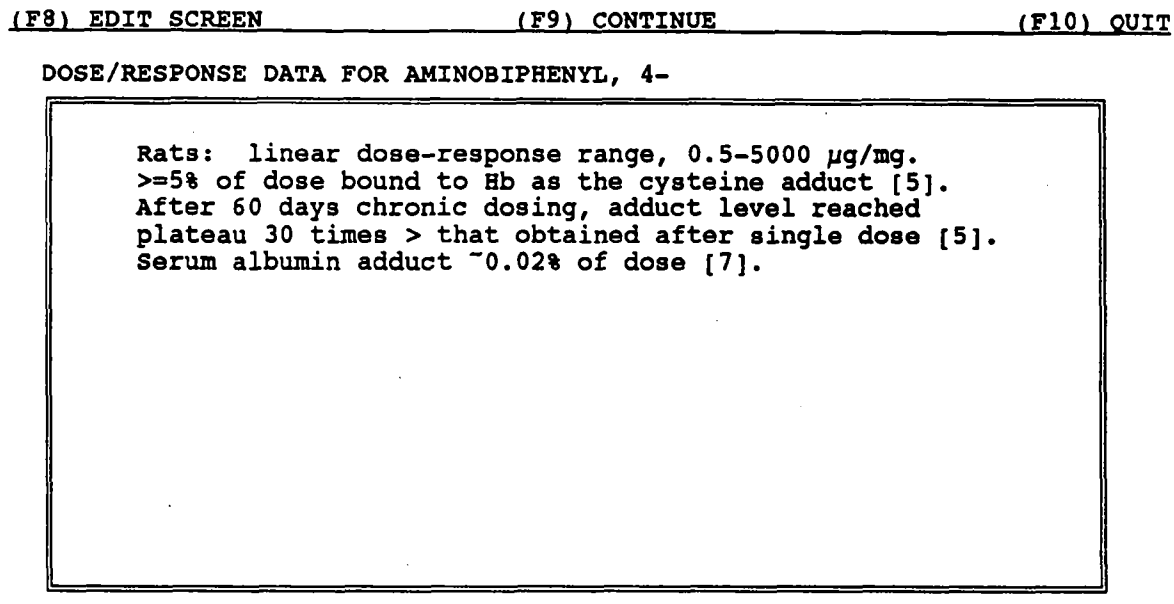
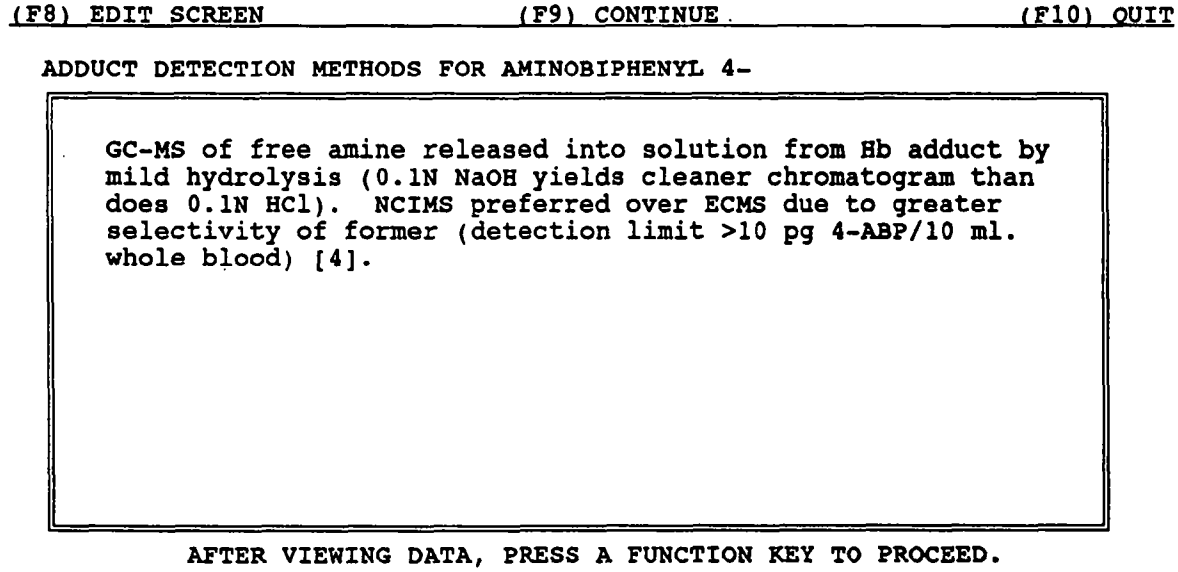


Figure 17 **The Dose-Response Data Screen**



igure 18 **The Adduct Detection Methods Screen**



MODIFYING THE DATABASE

THE ADD RECORD SCREEN

The ADD/DELETE MENU (Figure 20) appears on the screen when F8 is pressed while viewing the main menu. The ADD NEW RECORD SCREEN (Figure 21) is accessed by pressing "A" at the Add/Delete Menu. A new record is added to the database by entering a new chemical name and CAS number at the ADD NEW RECORD SCREEN. The new entry will not be alphabetized correctly unless the first character in the chemical name is a capital letter because, when DBASE™ sorts records alphabetically, it gives different values to uppercase and lowercase letters. However, CPAD averts this problem by automatically converting lowercase input to uppercase. It is extremely important, however, that the user place all leading numbers and/or greek letters at the end of the entry, separated by a comma (e.g., Aminobiphenyl,-4 rather than 4-Aminobiphenyl). Otherwise, the entry will not be correctly alphabetized in the sorted database upon the conclusion of the add session. Any error will be evident in the main menu listing.

After the new chemical name has been entered, the associated CAS number may also be entered in the format XXXXX-XX-X. No spaces are allowed....use zeros rather than blanks (e.g., 00092-67-1 rather than 92-67-1). A new record can be entered without including a CAS number, but this procedure is to be discouraged because it exempts the entry from the Duplicate Entry Protection Feature (Figure 22). When a CAS number is entered on the ADD NEW RECORD SCREEN, the program searches the database for that CAS number. If it is found, the program notifies the user accordingly and disallows the entry (Figure 22). Without such protection, the database could in time become cluttered with duplicate records for chemicals under one or more of their synonyms. If the entry is confirmed as a new CAS number, then the user is asked whether or not the data on the screen should be saved (Figure 23). A "NO" answer clears the ADD NEW RECORD SCREEN for another entry, while a "YES" answer saves the entries on screen and prompts the user for another entry (Figure 24).

Entering "N" at the prompt when all entries have been made will cause the modified database (i.e., the old records plus the newly appended ones) to be re-sorted alphabetically by chemical name to the backup database, LASTUPDT.DBF. Because this procedure takes a little time, it is performed only once per session, i.e., after all new records have been added. The un-sorted, modified database, SPADDUCT.DBF, is then deleted. The newly sorted database, LASTUPDT.DBF, is copied to the original filename, SPADDUCT.DBF, and the latter's index files, CAS.NDX and CHEM.NDX, are updated. LASTUPDT.DBF is retained as a backup. Heed the warning (Figure 25) to backup SPADDUCT.DBF regularly.

Figure 19 **The References Screen**

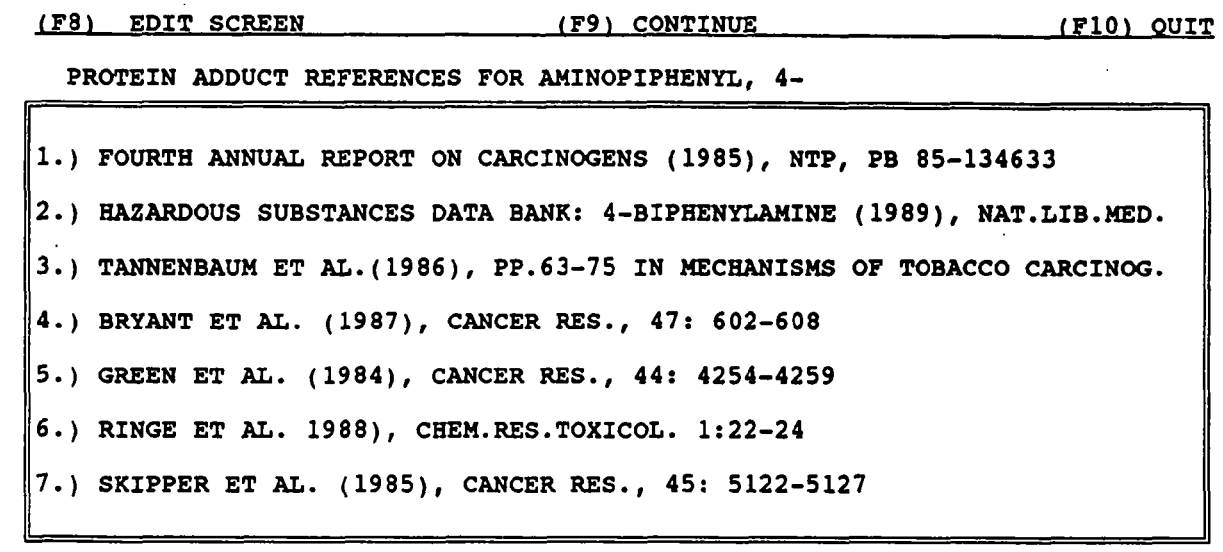


Figure 20 **The Add/Delete Menu**

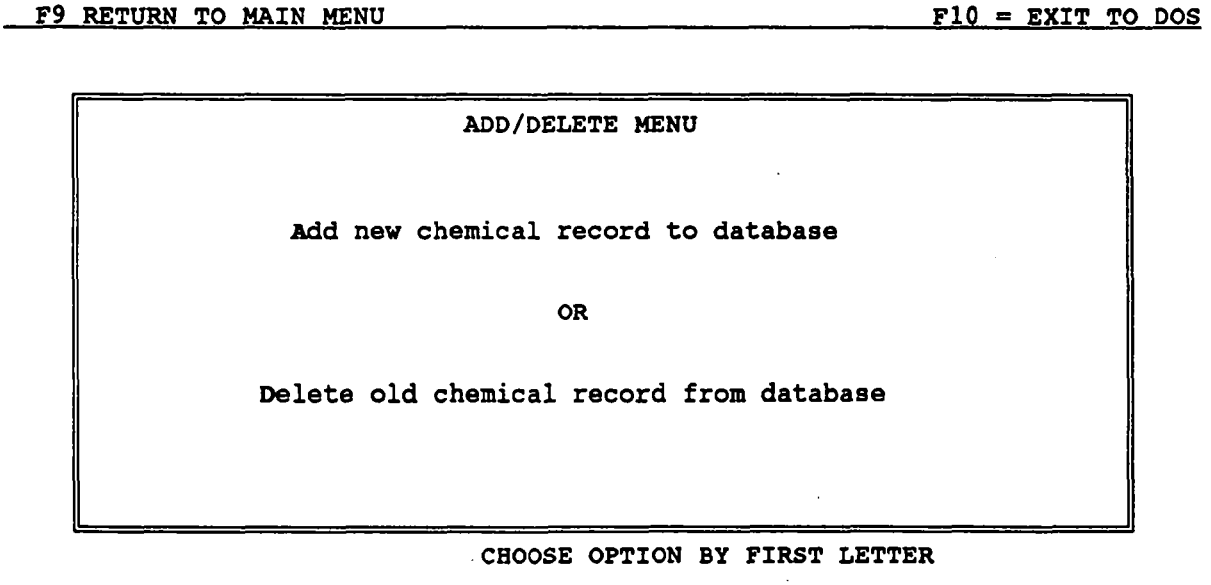


Figure 21 The Add New Record Screen

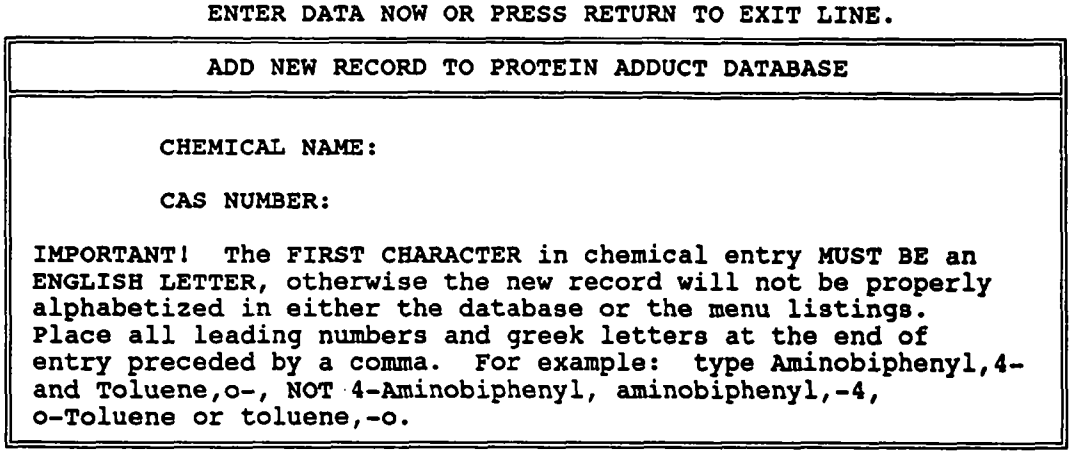


Figure 22 The Duplicate Entry Protection Feature

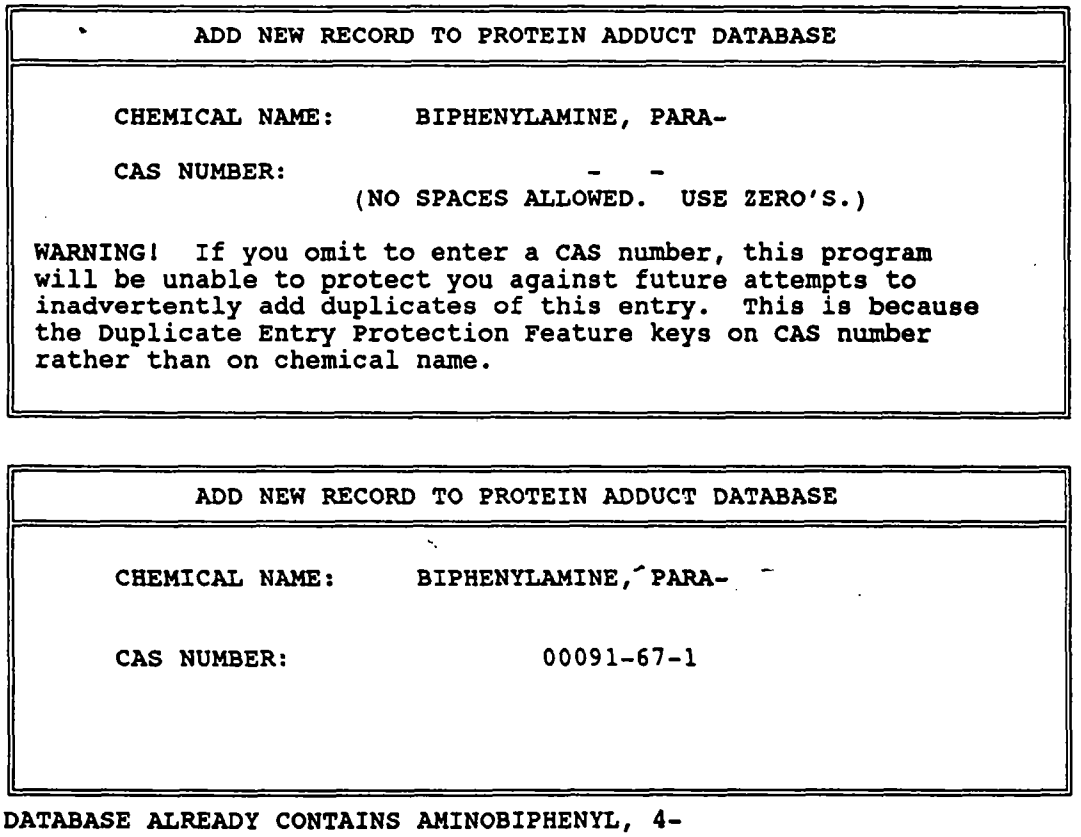


Figure 23 **The Save New Data Prompt**

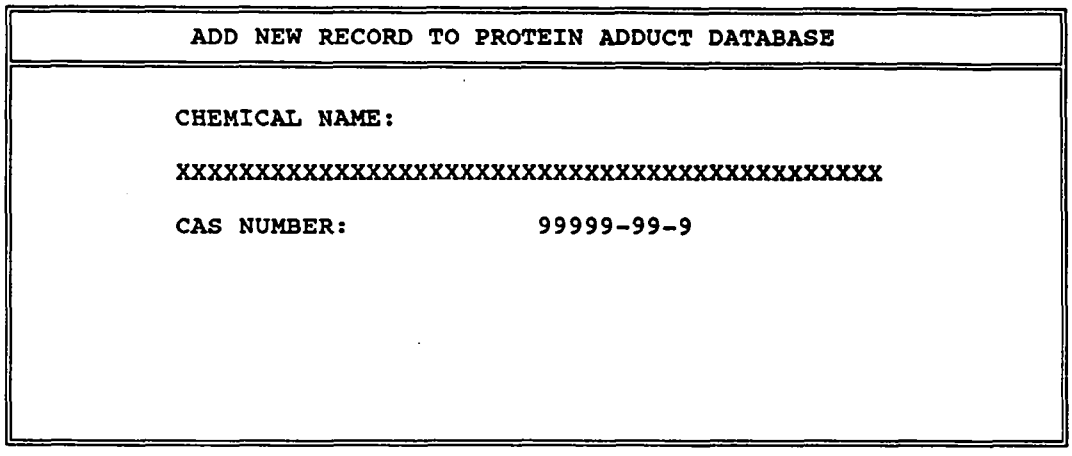


Figure 24 **The More/Done Prompt**

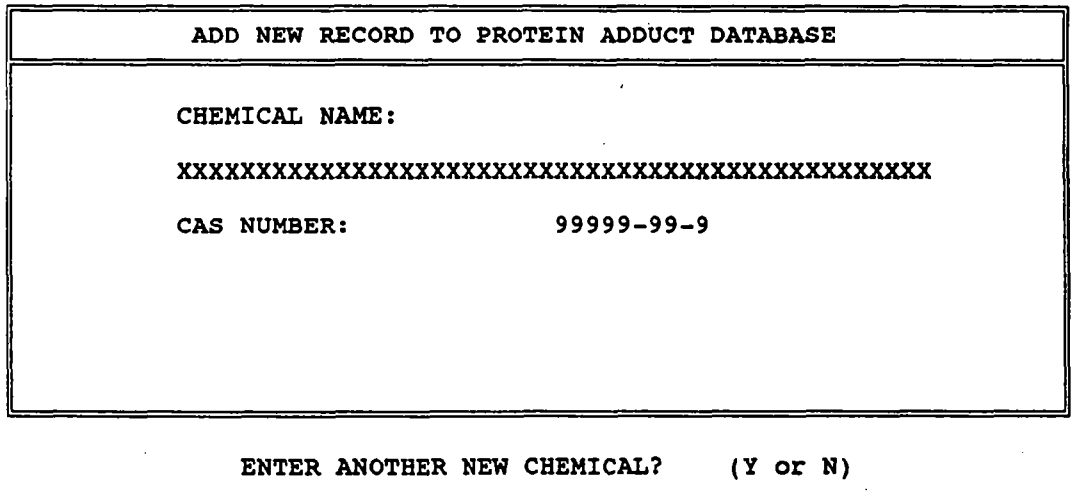
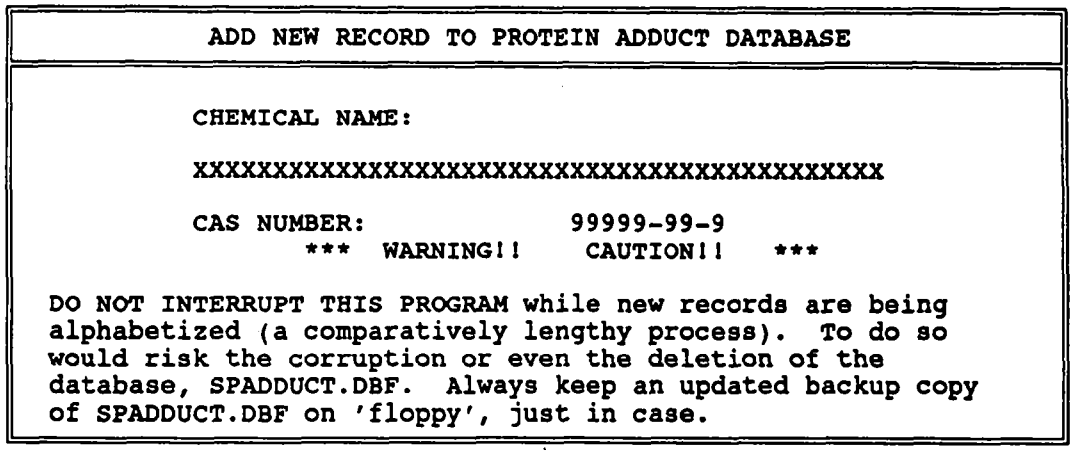


Figure 25 **The Re-Sort Database Prompt**

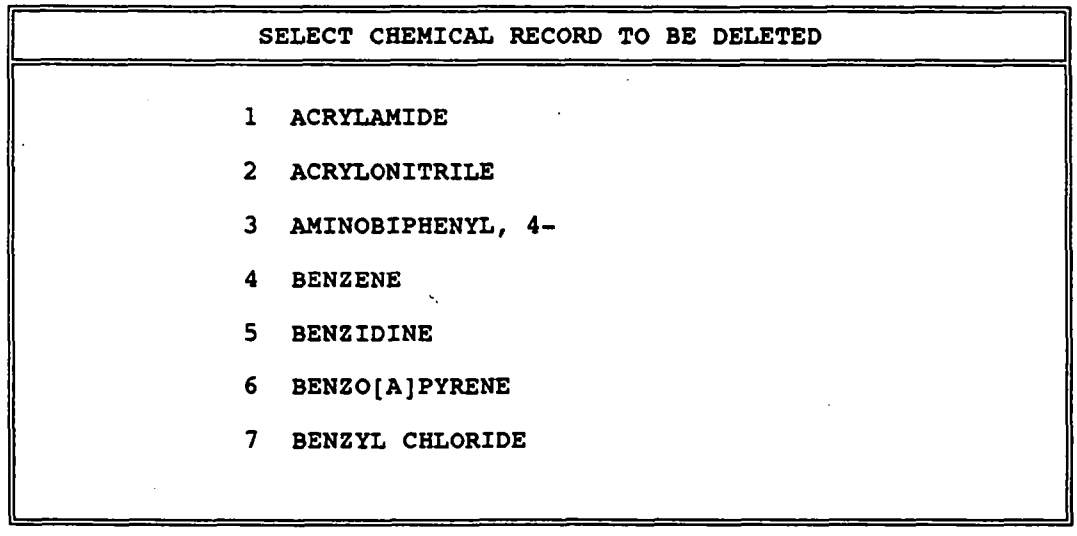


PLEASE WAIT WHILE ADDITIONS ARE ALPHABETIZED.

Figure 26 **The Delete Record Screen**

PGUP/PGDN = SCROLL F9 = RETURN TO MAIN MENU F10 = EXIT TO DOS

(THERE ARE A TOTAL OF 23 RECORDS TO VIEW.)



Press 1st letter in chemical name to 'jump' through listing or TYPE NUMBER of CHOICE (Press ENTER if <3 characters).

THE DELETE RECORD SCREEN

The DELETE RECORD SCREEN is used to delete one or more records from the database. It is accessed from the MAINMENU screen by pressing F8 for the ADD/DELETE MENU, then pressing "D" for the DELETE RECORD SCREEN (Figure 26). The latter works in exactly the same way that the MAINMENU screen does, except that it is used to select a chemical for deletion rather than for data display. First, the chemical is located, by entering the first letter in the chemical"s name and/or using the PGUP and PGDN keys (Figure 27). When a legal number is entered, the selection is identified at the bottom of the screen and the user is prompted to confirm his intention to delete that selection (Figure 28). A positive response (i.e., "Y") to the Selection Confirmation Prompt elicits the Deletion Confirmation Prompt "Are you sure? Deletion is forever, you know.". If the response is "Y", then CPAD proceeds to delete the selected record while notifying the user of both the action being taken, and the final result (Figure 29). If the response is "N", then CPAD asks the user if he/she wishes to delete another selection and, depending on the response, returns the user to either the beginning of the DELETE RECORD SCREEN or the ADD/DELETE MENU. A negative response (i.e., "N") to the Selection Confirmation Prompt elicits the prompt "Delete Another Selection? (Y or N)". A second negative response returns the user to the ADD/DELETE MENU; a positive response returns the user to the beginning of the DELETE RECORD SCREEN.

Since the relative order of the remaining records is unaffected by the deletion of one or more chemicals, it is not necessary to re-sort the database. However, it is necessary to re-index the database, i.e., to update the index files CHEM.NDX and CAS.NDX. Because it takes much less time to index a database than it does to sort a database, the record deletion routine of CPAD runs much faster than does its record addition routine.

THE FIELD EDIT SCREENS

While data deletion performed at the DELETE RECORD SCREEN is an all-or-nothing affair, only the Chemical Name and CAS Number for a new record can be entered at the ADD RECORD SCREEN. The remaining contents of a chemical record may be added/edited piecemeal at the appropriate FIELD EDIT SCREEN. The latter are accessed by pressing F8 (EDIT) at the corresponding data display screen. Apart from having grey backgrounds and highlighted input fields, any given FIELD EDIT SCREEN has the same "look and feel" as the corresponding DATA DISPLAY SCREEN. Most of the edit screens present either one or two fields and are driven by one of two programs, EDIT1FLD.PRG or EDIT2FLD.PRG. For reasons discussed below, three of the field edit screens, i.e., The CAS NUMBER EDIT SCREEN, the SYNONYMS EDIT SCREEN and the REFERENCES EDIT SCREEN, are driven by their own separate programs.

Figure 27 **The Locate Record Prompt**

PGUP/PGDN = SCROLL F9 = RETURN TO MAIN MENU F10 = EXIT TO DOS

(THERE ARE A TOTAL OF 23 RECORDS TO VIEW.)

SELECT CHEMICAL RECORD TO BE DELETED

23 XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

(END OF FILE)

Press 1st letter in chemical name to 'jump' through listing
or TYPE NUMBER of CHOICE (Press ENTER if <3 characters)

Figure 28 **The Selection Confirmation Prompt**

PGUP/PGDN = SCROLL F9 = RETURN TO MAIN MENU F10 = EXIT TO DOS

(THERE ARE A TOTAL OF 23 RECORDS TO VIEW.)

SELECT CHEMICAL RECORD TO BE DELETED

23 XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

(END OF FILE)

DELETE RECORD FOR XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX?
(Y or N)

Single-Field Screens

Eleven of the fifteen data display screens display the contents of a single field for the selected record. Of those, all but two (CASNUMBER and SYNONYMS) use the same procedure (EDIT1FLD.PRG) to format the screen. (The exceptions, MANUFACTURE, EXPOSURE, METABOLISM, CASNUMBER and SYNONYMS, are considered below under separate headings.)

The options mode of each edit screen is entered by pressing F8 (EDIT) at the desired data display screen (e.g., THE MAJOR ADDUCTS SCREEN). Upon entering the options mode of the edit screen (Figure 30), the data box is cleared and the user is given three options: (1) return to the data display screen by pressing F9, (2) view a help screen containing edit instructions by pressing F2, or (3) proceed to edit data by pressing F8 again.

The EDIT-HELP SCREEN is reproduced in Figure 31 and those instructions need not be repeated in full here. However, it is worth repeating that all the single-field edit screens governed by EDIT1FLD.PRG provide for self-formatting, unidirectional, multi-line input.

Upon entering the edit mode of the edit screen (Figure 32), the current data re-appears in the data box or window as highlighted input lines (NOTE: the highlighting does not show up in the figures), and the cursor is flashing at the beginning of the first line. Although it is the same data that appeared on the data display screen, it is probably not formatted the same. Recall (from the INSTALLATION AND STARTUP section) that those single-field data display screens that are governed by EDIT1FLD.PRG have their data automatically formatted by corresponding report form (.FRM) files. Edit each of the input lines as if they were all part of one long line (i.e., do NOT introduce extra spaces to avoid splitting a word between two lines). Also, remember that you cannot back up to correct errors made on a previous line. Instead, you will have to exit each line sequentially, return to the data display screen and start the editing process all over again. Therefore, spend time to save time by editing each line slowly and carefully. When all lines have been exited, save or abort the changes and return to the data display screen by giving the appropriate response at the prompt (Figure 33). When finished editing data, exit any remaining highlighted lines and save or abort changes by giving the appropriate response (Y or N) at the prompt.

Double-Field Screens

The MANUFACTURE, EXPOSURE and METABOLISM data display screens each display two fields in the same box or window. The associated edit screens, of which Figure 33 is an example, are

Figure 29 The Deletion Confirmation Prompt

```
PGUP/PGDN = SCROLL          F9 = RETURN TO MAIN MENU          F10 = EXIT TO DOS

              (THERE ARE A TOTAL OF 23 RECORDS TO VIEW.)
  +-----------------------------------------------------------------------+
  |                SELECT CHEMICAL RECORD TO BE DELETED                   |
  +-----------------------------------------------------------------------+
  |                                                                       |
  |          23   XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX    |
  |                                                                       |
  |                                                     (END OF FILE)     |
  +-----------------------------------------------------------------------+
    THE RECORD FOR XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
    HAS BEEN DELETED FROM THE DATABASE.
```

Figure 30 The Major Adducts Edit Screen-Options Mode

```
(F2) = HELP            (F8) = EDIT            (F9) = RETURN TO PREVIOUS SCREEN

    ADDUCTS FORMED BY AMINOBIPHENYL, 4-
  +-----------------------------------------------------------------------+
  |                                                                       |
  |                                                                       |
  +-----------------------------------------------------------------------+
                         SELECT ONE OF THE ABOVE
```

Figure 31 **The Edit-Help Screen**

EDIT - HELP SCREEN

WHEN ENTERING DATA, MAKE NO EFFORT TO FORMAT INPUT BEYOND ASSURING THAT THERE IS A SPACE BETWEEN EVERY WORD AND SENTENCE. ESPECIALLY, DO NOT TRY TO "WRAP AROUND" DATA AS IT IS ENTERED BY ADDING SUPERFLUOUS SPACES OR OMITTING OTHERS. THE INPUT WILL BE AUTOMATICALLY FORMATTED BY THE APPROPRIATE DATA DISPLAY SCREEN. IF, FOR EXAMPLE, A WORD ON THE EDIT SCREEN BEGINS ON THE LAST PART OF ONE LINE AND ENDS ON THE FIRST PART OF THE NEXT LINE, IT WILL "WRAP AROUND" PROPERLY ON THE DATA DISPLAY SCREEN. IF, HOWEVER, A WORD ENDS ON THE LAST SPACE OF AN EDIT LINE, THE NEXT LINE MUST BEGIN WITH A SPACE RATHER THAN WITH THE NEXT WORD. OTHERWISE, ON THE SELF-FORMATTING DATA DISPLAY SCREEN, THE TWO WORDS WILL APPEAR AS A SINGLE WORD.

WHEN ONE LINE IS FILLED, THE CURSOR WILL AUTOMATICALLY JUMP TO THE NEXT LINE. HOWEVER, IF YOU WISH TO SKIP A LINE WITHOUT CHANGES, OR YOU FINISH YOUR ENTRY BEFORE THE LINE HAS BEEN FILLED, THEN YOU MUST PRESS <RETURN> OR THE DOWN ARROW IN ORDER TO PROCEED TO THE NEXT LINE, FIELD, OR PROMPT. ONCE BEGUN, THE EDIT PROCESS CANNOT BE INTERRUPTED. TO EXIT THE EDIT MODE, YOU MUST PRESS <RETURN> AT EACH AND EVERY ONE OF THE REMAINING UNEDITED LINES. JUST FOLLOW DIRECTIONS ON THE SCREEN FOR CAS NUMBER, SYNONYMS, AND REFERENCES. EACH OF THESE SCREENS HAS ITS OWN SPECIAL EDITING PROGRAM.

(END OF HELP SCREEN)

PRESS ANY KEY TO RETURN TO EDIT SCREEN...

Figure 32 **The Major Adducts Edit Screen-Edit Mode**

EDIT SCREEN AT CURSOR, OR PRESS <RETURN> TO EXIT LINE.

ADDUCTS FORMED BY AMINOBIPHENYL, 4-

(DNA): N-(deoxyguanosin-8-yl)-ABP [2]. (Protein): Sulfonamide adduct at the beta-93 cysteine residue of hemoglobin [5,6], and 3-Tryptophan-N1-yl)-4-acetyl-ABP adduct at the Trp-214 residue of Serum albumin [7].

MAKE DESIRED CHANGES, THEN PRESS RETURN.

governed by one procedure file (EDIT2FLD.PRG). They work the same way that single-field edit screens do, except that the flashing cursor jumps immediately from the bottom of the first field to the top of the second. Be careful that data from the first field does not overflow into the second field.

The CAS Number and Synonyms Screens

The single-field edit screens CAS NUMBER and SYNONYMS are each governed by their own separate procedure files (CASEDIT.PRG and SYNEDIT.PRG), but they work the same way that the other edit screens do. The CASNUMBER EDIT SCREEN (Figure 34) contains a single input line and will accept only numbers as input (use zeros in lieu of leading blanks).

The SYNONYMS EDIT SCREEN (Figure 35) displays six input lines, one for each of up to six different synonyms for the selected chemical name. In the database, all the synonyms for a chemical are contained in a single field and separated by semicolons. As a result, it is important to avoid the accidental entry of semicolons when editing data in the synonyms field. Portions of a single input line separated by semicolons will be formatted on the data display screen as separate synonyms.

The References Screen

The REFERENCES EDIT SCREEN (Figure 36) displays seven input lines. However, these input lines, unlike those of the SYNONYMS screen, represent seven separate fields, one for each of a maximum of seven citations. The separate procedure file (REFSEDIT.PRG) that governs this screen differs from the others in that it allows the user to randomly edit and re-edit lines within a single edit session. This means that one can back up to correct input errors in lines already exited without having to exit the edit mode and start all over, again.

The references are limited to seven citations per chemical for two reasons. First, all the CPAD data are contained in a single database file (SPADDUCTS.DBF) for convenience. Each chemical record already consumes the maximum storage space allowed within the structural limitations of DBASE™, i.e., without splitting the database up into multiple files. Second, CPAD was not designed to provide the detail that is more properly sought in the scientific literature. Rather, it is intended to concisely indicate the status of fundamental research on protein adduct-forming chemicals as relates to their potential for exposure monitoring. Also, the reference fields, which will be continually updated along with the rest of CPAD's data fields, should always include recent review articles or research papers that can provide the basis of a larger literature search.

Figure 33 **The Exposure Data Edit Screen-Save Prompt**

EDIT SCREEN AT CURSOR, OR PRESS <RETURN> TO EXIT LINE.

EXPOSURE DATA FOR AMINOBIPHENYL, 4-

SOURCES OF EXPOSURE	LEVELS OF EXPOSURE
Cigarette smoke and other combustion products. Certain azo dyes contain 4-ABP as a contaminant and may release more on metabolism.[2]	Nanogram amounts in cigarette smoke. Trace amounts in certain azo dyes such as FD&C Yellow #5 and #6. 4-ABP and 4-Nitrobiphenyl (which yields 4-ABP upon enzymatic nitroreduction) may occur in a number of combustion products. [2]

SAVE CURRENT CHANGES, NOW? (Y or N)

Figure 34 **The CAS Number Edit Screen**

ENTER NUMBERS ONLY, SPACES NOT ALLOWED, USE ZEROS INSTEAD.

CAS NUMBERS FOR AMINOBIPHENYL, 4-

00092-67-1

MAKE DESIRED CHANGES, THEN PRESS RETURN.

Figure 35 **The Synonyms Edit Screen**

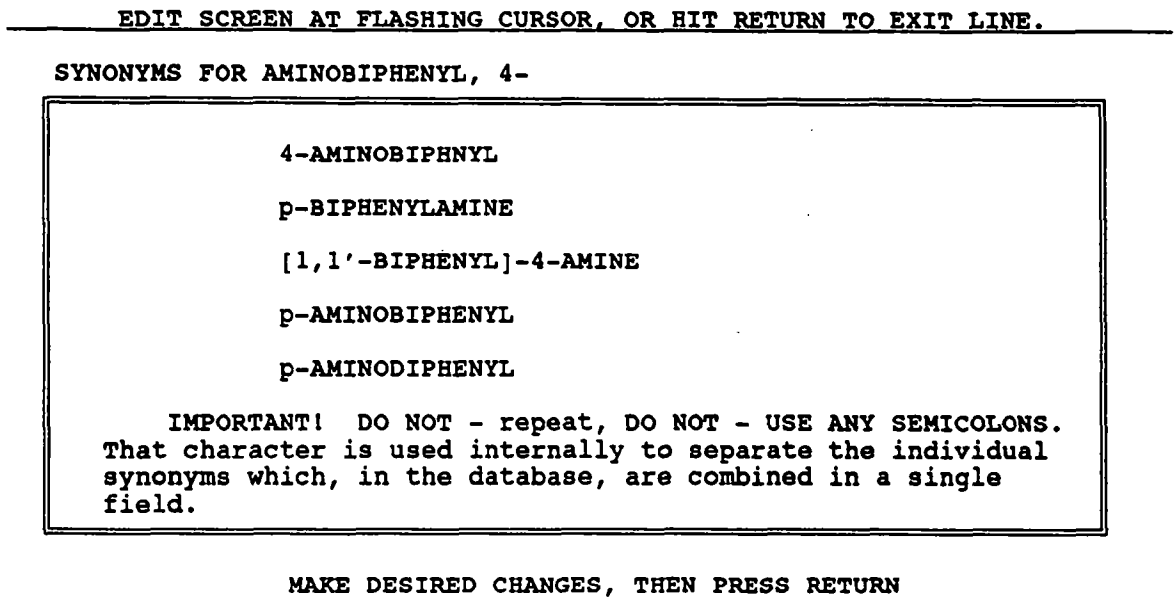
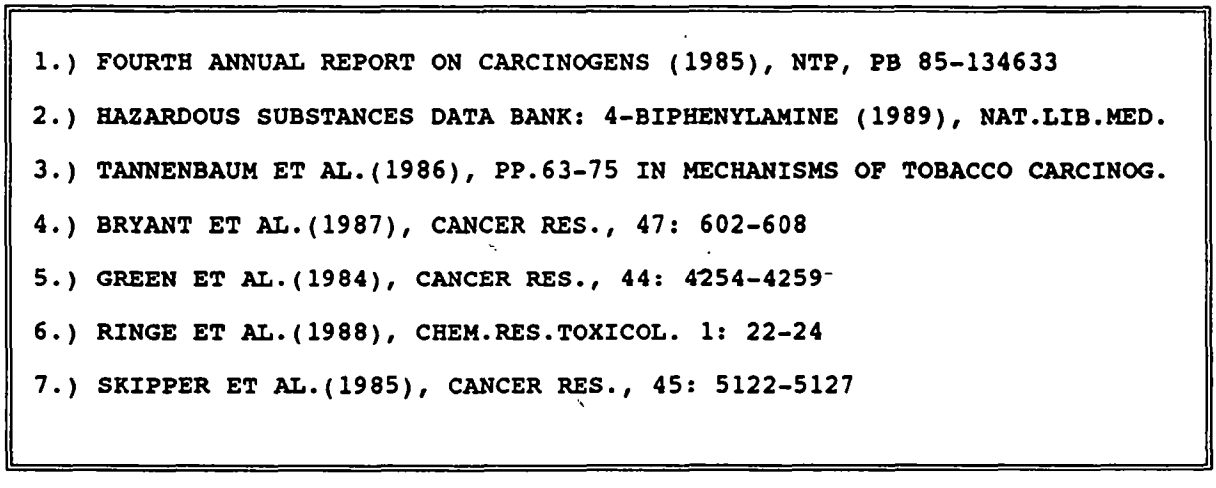


Figure 36 **The References Edit Screen**



REFERENCES

Carribis, Joseph-David (1987). DBASE™ III PLUS: The Complete Reference, Osbourne McGraw Hill, Berkeley, California.

Liskin, Miriam (1988). Advanced DBASE™ III PLUS: Programming and Techniques, Osbourne/McGraw Hill, Berkeley, California.

Schnell, Frank C. (1989). Protein Adduct-Forming Chemicals for Exposure Monitoring: Chemicals Selected for Further Study, EPA 600/4-89/035.

APPENDIX A

THE DATABASE STRUCTURE OF CPAD

Structure for database: C:SPADDUCT.DBF
Number of data records: 22*
Date of last update : 08/21/90

Field	Field Name	Type	Width
1	CASNUMBER	Character	10
2	CHEMICAL	Character	46
3	SYNONYMS	Character	235
4	MFGVOLUME	Character	68
5	MANUFACTUR	Character	254
6	USES	Character	254
7	EXPOSOURCE	Character	136
8	EXPOSURE	Character	254
9	HEALTHFX	Character	254
10	DETOX	Character	254
11	ACTIVATION	Character	254
12	HOSTFACTOR	Character	254
13	ELECTROPHI	Character	204
14	ADDUCTS	Character	254
15	RATECNSTNT	Character	68
16	BACKGROUND	Character	204
17	DOSERESPON	Character	254
18	METHOD	Character	254
19	REF1	Character	68
20	REF2	Character	68
21	REF3	Character	68
22	REF4	Character	68
23	REF5	Character	68
24	REF6	Character	68
25	REF7	Character	68
26	BLANK	Character	1

Total bytes per record = - 3989

* Inquiries regarding the availability of updates of SPADDUCTS.DBF should be directed to Charles H. Nauman at the following address: United States Environmental Protection Agency, Environmental Monitoring Systems Laboratory, Exposure Assessment Research Division, P.O. Box 93478, Las Vegas, NV, 89193-3478.

APPENDIX B

CHEMICALS IN CPAD DATABASE AS OF MARCH 1991

The 22 chemicals listed below represent those chemicals of interest to the EPA that were identified as having potential for exposure monitoring using protein adduct measurements (EPA 600/4-89/035, Oct., 1989). Future updates of CPAD (i.e., of the primary database file SPADDUCTS.DBF') will contain more data on more chemicals, reflecting the rapid growth of research in molecular dosimetry.

Record#	chemical
1	ACRYLAMIDE
2	ACRYLONITRILE
3	AMINOBIPHENYL, 4-
4	BENZENE
5	BENZIDINE
6	BENZO[a]PYRENE
7	BENZYL CHLORIDE
8	CHLOROFORM
9	DIMETHYLBENZANTHRACENE, 7,12-
10	EPICHLORHYDRIN
11	ETHYLENE DICHLORIDE
12	ETHYLENE OXIDE
13	FORMALDEHYDE
14	METHYLENE BIS(2-CHLOROANILINE), 4,4'- , (MOCA)
15	NITROPYRENE, 1-
16	NITROSONORNICOTINE
17	PENTACHLOROPHENOL
18	PROPYLENE OXIDE
19	STYRENE
20	TOLUENE DIISOCYANATE, 2,4-
21	TOLUIDINE, o-
22	VINYL CHLORIDE

Inquiries regarding the availability of updates of SPADDUCTS.DBF should be directed to Charles H. Nauman at the following address: United States Environmental Protection Agency, Environmental Monitoring Systems Laboratory, Exposure Assessment Research Division, P.O. Box 93478, Las Vegas, NV, 89193-3478.

APPENDIX C

CPAD FILES: THE DBASE™ III PLUS VERSION

If DBASE™ III PLUS is installed on your computer, only the files located under the CPAD.DB3 directory of the CPAD diskette (listed below) need be transferred to a separate directory (e.g., C:\CPAD) on your hard drive. If DBASE™ III PLUS is not installed on your computer, then all three DBRUN files from the RUNTIME.DB3 directory must also be copied to C:\CPAD. On-screen installation instructions are provided in the README files.

Filename	Bytes	Description:
README DB3	1255	Installation information.
README DB4	1485	Installation information.
README BAT	63	Displays README Files.
CPAD.DB3 <DIR>:		
START BAT	778	Startup Batch File.
TITLSCRN EXE	7774	Opening graphics screen.
WAITMSG TXT	401	Loading Message
PADDUCTS PRG*	36256	Main Program.
BACKGRND FRM	1990	Data display form.
ADCTFRMD FRM	1990	" " "
D-R FRM	1990	" " "
RCTVMTBL FRM	1990	" " "
RATECNST FRM	1990	" " "
MFG FRM	1990	" " "
METHODS FRM	1990	" " "
EXPOSURE FRM	1990	" " "
METAB FRM	1990	" " "
SYNONYMS FRM	1990	" " "
USES FRM	1990	" " "
HEALTHFX FRM	1990	" " "
HOSTFCTR FRM	1990	" " "
SPADDUCT DBF	89088	The Primary Database.
LASTUPDT DBF	92613	Backup Database.
SPADDNEW DBF	4855	Temporary Append Database.
CHEM NDX	2560	Alphabetizes Chemicals.
CASNUM NDX	1024	Cas Number Index.
EOS EXE	7286	End of Session Screen.
SRCCODE DB3 <DIR>*		Contains Source Code.
OBJCODE DB3 <DIR>*		Contains 32 object files.
USERSMAN.UAL <DIR>		Contains Users'Manual.
RUNTIME.DB3 <DIR>		Contains 3 DBRUN Files: DBRUN.MSG, DBRUN.OVL, AND DBRUN.EXE.

*PADDUCTS.PRG was developed from the files in the SRCCODE.DB3 and OBJCODE.DB3 directories. These files, which are listed on the next page, are not required to run CPAD. They are included only for users who may be interested in program development.

Thirty two original DBASE™ III PLUS Program files were written (left-hand column below). These files were compiled using the DBASE™ utility DBC.COM. The compressed files (right-hand column below) were then linked together using the DBASE™ utility DBL.COM, to form the single object file, PADDUCTS.PRG.

Directory of A:\SRCCODE.DB3

Filename	Bytes
MAINMENU SRC	4456
ADDELMNU SRC	910
SPADD SRC	4728
SPADDEL SRC	4346
DELPAK SRC	1211
CHMORPAD SRC	1005
CFLDMENU SRC	1940
PFLDMENU SRC	1943
CASNUMBR SRC	1153
CASEDIT SRC	2364
MFG SRC	1710
EXPOSURE SRC	1694
METAB SRC	1728
SYNONYMS SRC	1347
SYNEDIT SRC	3367
USES SRC	1559
HEALTHFX SRC	1531
HOSTFCTR SRC	1531
VIEWALLC SRC	552
RCTVMTBL SRC	1544
RATECNST SRC	1561
DOSERSPN SRC	1548
ADCTFRMD SRC	1554
BACKGRND SRC	1594
METHODS SRC	1560
PADREFS SRC	1324
REFSEDIT SRC	2931
EDIT1FLD SRC	3838
EDIT2FLD SRC	4330
VIEWALLP SRC	548
VIEWALL SRC	612
HELPMSG SRC	1634

Directory of A:\OBJFILE.DB3

Filename	Bytes
MAINMENU PRG	2048
ADDELMNU PRG	602
SPADD PRG	3149
SPADDEL PRG	1956
DELPAK PRG	714
CHMORPAD PRG	633
CFLDMENU PRG	1337
PFLDMENU PRG	1359
CASNUMBR PRG	685
CASEDIT PRG	1446
MFG PRG	1106
EXPOSURE PRG	1094
METAB PRG	1095
SYNONYMS PRG	827
SYNEDIT PRG	2096
USES PRG	934
HEALTHFX PRG	952
HOSTFCTR PRG	954
VIEWALLC PRG	226
RCTVMTBL PRG	957
RATECNST PRG	960
DOSERSPN PRG	958
ADCTFRMD PRG	938
BACKGRND PRG	977
METHODS PRG	965
PADREFS PRG	816
REFSEDIT PRG	1866
EDIT1FLD PRG	1806
EDIT2FLD PRG	1985
VIEWALLP PRG	224
VIEWALL PRG	294
HELPMSG PRG	1514

The remaining directories (CPAD.411, SRCCODE.411 and OBJCODE.411) on the CPAD diskette contain files that relate to a version of CPAD that can only be used on computers that have DBASE™ IV, version 1.1, installed on the hard drive. These files are listed in Appendix D.

APPENDIX D

CPAD FILES: THE DBASE™ IV VERSION

If you have DBASE™ IV version 1.1 on your hard disk, then only the contents of the CPAD.411 directory of the CPAD diskette need be copied to a separate directory (e.g., C:\CPAD) on your hard drive. A stand-alone DBASE™ IV (1.1) version of CPAD is not provided on the CPAD diskette because it would require three times as much disk space as the DBRUN III PLUS version and still would not run as well. Listed below are the contents of the directories containing DBASE™ IV ver.1.1 CPAD files.

Note that the primary database file SPADDUCTS.DBF is identical in both CPAD versions. Thus, for current users of CPAD (regardless of version), future updates of CPAD need consist of only one file. Such updates, when available, may be obtained by contacting Charles H. Nauman at the following address: United States Environmental Protection Agency, Environmental Monitoring Systems Laboratory, Exposure Assessment Research Division, P.O. Box 93478, Las Vegas, NV, 89193-3478.

Filename		Bytes	Description:
CPAD.411 <DIR>:			
START	BAT	62	Startup Batch File.
WAITMSG	TXT	398	Loading Message
IBMPRO_1	PR2	808	Printer Driver
PRNTFRM	PRF	698	Print format file
TITLSCRN	EXE	7792	Opening Graphics Screen.
MAINMENU	DBO*	118636	Main Program
SPADDUCT	DBF	88624	The Primary Database.
SPADDNEW	DBF	4854	Temporary Append Database.
LASTUPDT	DBF	88624	Backup Database.
CHEM	NDX	2560	Alphabetizes Chemicals.
CASNUM	NDX	1024	Cas Number Index.
EOS	EXE	7286	End of Session Screen.
SRCCODE.411 <DIR>:*			Contains Source code
OBJCODE.411 <DIR>:*			Contains unlinked Object Code Files.

*MAINMENU.DBO was developed from the files in the SRCCODE.411 and OBJCODE.411 directories. These files, which are listed on the next page, are not required to run CPAD, but are included for those users who may be interested in program development.

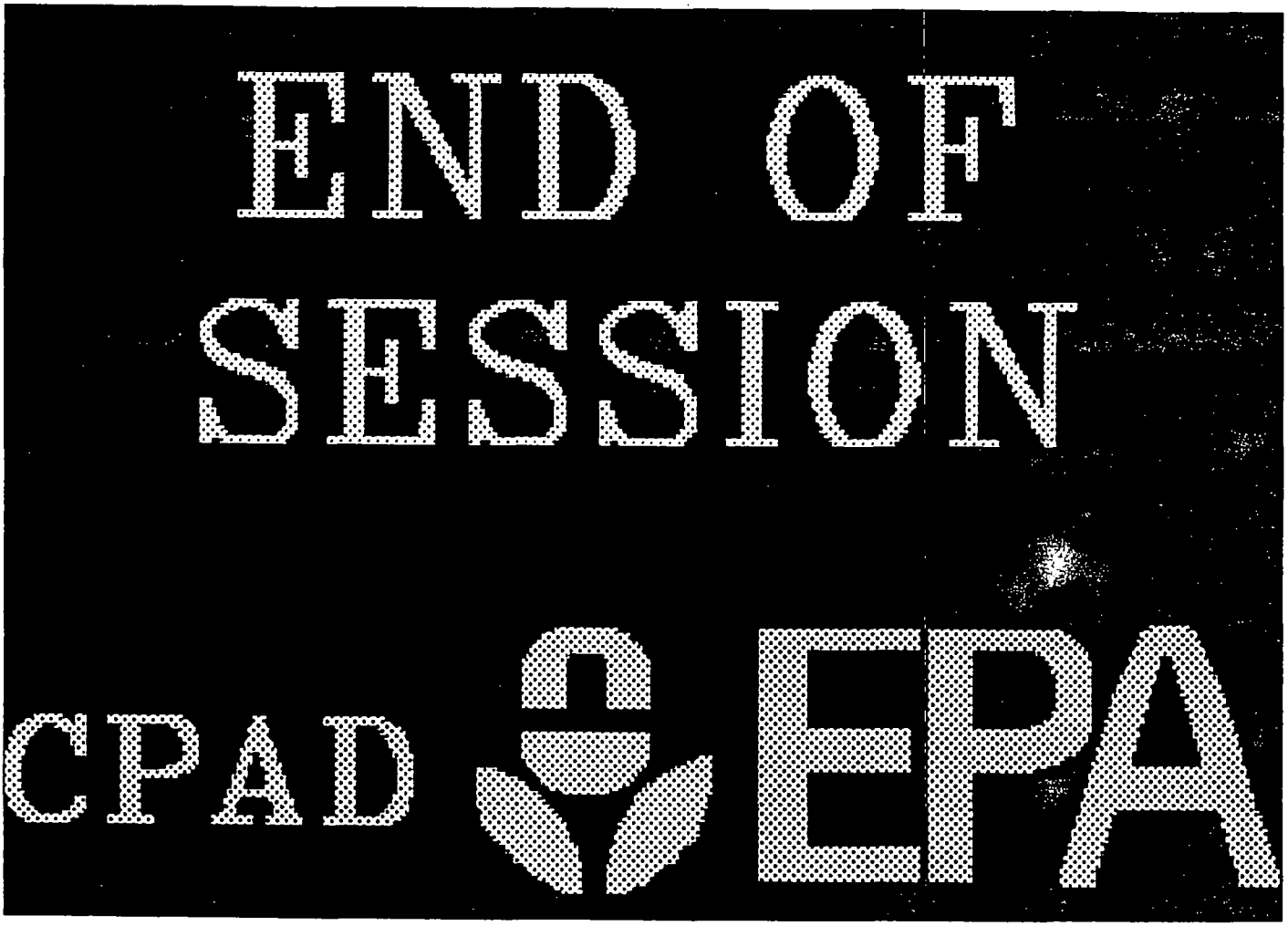
APPENDIX D (Continued)

Directory of A:\SRCCODE.411

Filename		Bytes
MAINMENU	PRG	4347
SPADD	PRG	4708
SPADDEL	PRG	4346
DELPAK	PRG	1211
METAB	PRG	1807
CASEDIT	PRG	2433
RATECNST	PRG	1640
HELPMSG	PRG	1634
EXPOSURE	PRG	1773
BACKGRND	PRG	1636
EDIT1FLD	PRG	3845
VIEWALLC	PRG	552
PADREFS	PRG	1385
ADDELMNU	PRG	910
SYNONYMS	PRG	1408
SYNEDIT	PRG	3395
CHMORPAD	PRG	1005
CFLDMENU	PRG	1940
PFLDMENU	PRG	1943
CASNUMBR	PRG	1172
HOSTFCTR	PRG	1585
ADCTFRMD	PRG	1598
METHODS	PRG	1639
MFG	PRG	1786
EDIT2FLD	PRG	4331
VIEWALLP	PRG	548
VIEWALL	PRG	612
REFSEDIT	PRG	2905
HEALTHFX	PRG	1610
USES	PRG	1591
RCTVMTBL	PRG	1623
DOSERSPN	PRG	1627
RCTVMTBL	FRM	1084
HEALTHFX	FRM	1084
MFG	FRM	1460
METAB	FRM	1299
EXPOSURE	FRM	1450
USES	FRM	1080
HOSTFCTR	FRM	1084
RATECNST	FRM	1084
ADCTFRMD	FRM	1084
BACKGRND	FRM	1084
DOSERSPN	FRM	1084
METHODS	FRM	1083

Directory of A:\OBJCODE.411

Filename		Bytes
MAINMENU	DBO	3976
CHMORPAD	DBO	1296
CFLDMENU	DBO	2616
SPADDEL	DBO	3996
MFG	DBO	2448
HEALTHFX	DBO	2140
EXPOSURE	DBO	2428
USES	DBO	2124
EDIT1FLD	DBO	3836
RCTVMTBL	DBO	2152
HOSTFCTR	DBO	2104
HELPMSG	DBO	1884
METAB	DBO	2440
EDIT2FLD	DBO	4236
RATECNST	DBO	2156
SYNONYMS	DBO	1992
SYNEDIT	DBO	4076
CASNUMBR	DBO	1564
CASEDIT	DBO	2880
VIEWALLC	DBO	820
ADDELMNU	DBO	1104
SPADD	DBO	4916
DELPAK	DBO	1416
PFLDMENU	DBO	2624
ADCTFRMD	DBO	2140
BACKGRND	DBO	2160
DOSERSPN	DBO	2164
METHODS	DBO	2172
PADREFS	DBO	1988
REFSEDIT	DBO	3532
VIEWALLP	DBO	812
VIEWALL	DBO	1044
EXPOSURE	FRO	3840
MFG	FRO	3844
METAB	FRO	3808
HEALTHFX	FRO	3684
USES	FRO	3684
HOSTFCTR	FRO	3684
RCTVMTBL	FRO	3684
RATECNST	FRO	3684
ADCTFRMD	FRO	3684
BACKGRND	FRO	3684
DOSERSPN	FRO	3684
METHODS	FRO	3684


END OF
SESSION
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PROJECT SUMMARY

USER'S GUIDE

COMPUTERIZED PROTEIN ADDUCTS DATABASE (CPAD)

Frank C. Schnell and Charles H. Nauman

ABSTRACT

This user's manual contains directions for the installation and use of the computerized Protein Adducts Database (CPAD). Most of this documentation is also available on-screen in the form of CPAD's "Readme" files and program prompts. CPAD, a user-friendly, menu-driven, stand-alone DBASE™ application, was created to provide an efficient means of updating and disseminating information on protein adducts relating to their utility as dosimeters of exposure to environmental contaminants, especially genotoxic and/or carcinogenic compounds. The structure of the database as well as its initial contents were derived primarily from the document, "Protein Adduct-Forming Chemicals for Exposure Monitoring: Chemicals for Further Study" (EPA/600/4-89/035).

Software for executing CPAD accompanies the User's Guide on a single high density 3.5" diskette. The diskette contains (1) two versions of CPAD that run with DBASE™ III PLUS and DBASE™ IV, version 1.1, respectively, (2) the DBRUN™ files needed to run CPAD as a stand-alone DBASE™ III PLUS application, (3) a copy of the User's Manual (a WORDPERFECT™ 5.0 document file) which may be viewed on screen or printed out, and (4) the source

code and unlinked object code files used to develop CPAD's main program. The latter files are not required to run CPAD and are included only for the information of users who may be interested in the program's design. See the back of this Project Summary for ordering information.

INFORMATION

The U.S. Environmental Protection Agency (EPA) has developed an initiative designed to develop, refine and apply appropriate biomarkers for use in conjunction with environmental monitoring data to provide better estimates of exposure and risk to individuals and populations. Among the biomarkers under study are macromolecular adducts formed in vivo by reactive environmental chemicals or their metabolites.

A report entitled "Protein Adduct-Forming Chemicals For Exposure Monitoring: Literature Summary and Recommendations" (EPA/600/4-90/007) summarized the literature regarding adducts formed by xenobiotics with proteins, particularly hemoglobin and serum albumin, and examined the feasibility of their use as dosimeters of exposure. Twenty-two chemicals of interest to the EPA were recommended for further study and ranked according to their potential utility in exposure monitoring by protein adduct-based methods. These prioritized chemicals were then examined in greater detail in a report entitled "Protein Adduct-Forming Chemicals For Exposure Monitoring: Chemicals Selected for Further Study" (EPA/600/4-89/035).

It was anticipated that, due to rapid developments in the field of molecular dosimetry, the information in the last-mentioned protein adducts report, as well as the prioritized chemicals list, itself, would require frequent amendments and updates in the future. To facilitate that process, the Computerized Protein Adducts Database (CPAD) was developed. The structure of the database as well as its initial contents were derived primarily from the last-mentioned project report (EPA/600/4-89/035). The database includes entries on the following topics: manufacture and use, sources and levels of exposure, known health effects, metabolism (detoxification and activation), host factors, reactive metabolites, adduct characterization, rates of adduct formation (i.e., second order rate constants), background adduct levels, dose-response relationships, and methods of adduct detection.

PROCEDURE

CPAD is intended to run on an IBM-compatible PC with hard disk under DOS. It can be run from a 3.5" drive, but this is not recommended, as program execution is slowed down considerably.

The DBASE™ III PLUS version

This version of CPAD may be used with or without DBASE™ III PLUS. If your computer has DBASE™ III PLUS installed, only the files in the CPAD.DB3 Directory of the 3.5" CPAD diskette need be copied to a separate subdirectory on your hard drive (e.g., c:\CPAD). These files will require approximately 270 K of

memory. If your computer does not have DBASE™ III PLUS installed, then the three DBRUN files provided must also be copied into the CPAD directory on your hard disk. The resulting stand-alone version of CPAD requires a total of 605 K.

The DBASE™ IV (1.1) version

For the benefit of those who have DBASE™ IV, version 1.1, installed on their computers, a compatible version of CPAD has been included on the CPAD diskette. To install this version of CPAD, simply copy all the files from the CPAD.411 directory of the CPAD diskette to a separate directory on your hard drive (e.g.,c:\CPAD). You will need only about 325 KB of disk space for the DBASE™ IV version. A stand-alone (Runtime) DBASE™ IV, 1.1 version of CPAD is not included, because it would require a million bytes more than does the stand-alone DBASE™ III PLUS version.

OPERATION

Getting Started

To run either version of CPAD, simply enter "START" from within the subdirectory that contains the CPAD files (and the three DBRUN files, in the stand-alone version). Alternatively, the compatible version of CPAD may be run from within DBASE™ III PLUS or DBASE™ IV by entering "DO PADDUCTS" or "DO MAINMENU", respectively, at the dot prompt, provided that (1) DBASE™ is loaded from within your CPAD directory, thereby making it the

default directory, and (2) the DBASE™ directory is in your PATH statement.

SEARCHING THE DATABASE

The main menu of CPAD is a scrolling, alphabetical list of chemicals for which records exist in CPAD. When a chemical is selected, the main menu closes and the field-selection menu opens. The user may choose one of three options: (1) view only those fields containing information on the selected chemical, (2) view only those fields containing information on the protein adducts formed by the chemical, or (3) browse through all the data fields on the selected chemical. Chemical Data Fields include CAS Number, Synonyms, Volume and Method of Manufacture, Major Uses, Sources and Levels of Exposure, Health Effects, Metabolism, and Host Factors. Protein Constant Adduct Data Fields include Reactive Metabolites, Adducts Formed, (second order) Rate Constant (of formation), Background Levels (of adducts), Dose-Response Data, Methods of Detection, and References. After selecting 1 or 2 above, the user may select to view individual data screens or browse through all data screens (i.e., Chemical or Protein Adduct) in sequence.

Modifying the Database

Existing data on a selected chemical may be edited/updated at the appropriate data screen by entering Edit Mode. The Delete Menu works the same way the Main Menu does, except that the entire record for the selected chemical is deleted if the user's

intent to do so is confirmed at the prompt. The Add Menu allows the user to add new records (i.e., chemicals and CAS numbers, only). A Duplicate Entry Protection Feature keys on CAS number rather than chemical name. Any new chemical names added at the Add Menu will subsequently appear in the alphabetical listing at the Main Menu. All other data for new records is keyed in at the individual data display screens in input mode, after selecting the new chemical at the Main Menu.

SOFTWARE AVAILABILITY

The Computerized Protein Adducts Database (CPAD) can be obtained by sending a single, formatted, high-density (1.44 MB), 3.5" diskette to the following address:

Dr. Charles H. Nauman
U.S. E.P.A., EMSL, MC-EAD
P.O. Box 93478
Las Vegas, NV 89193-3478

The CPAD Software, the accompanying User's Manual, and the aforementioned protein adducts project reports EPA 600/4-90/007 and EPA/600/4-89/035 were written by Dr. Frank C. Schnell. He may be contacted at the following address:

Lockheed Engineering and Sciences Co.
1050 E. Flamingo Rd.
Las Vegas, NV 89119

INFORMATION BOX (for use by CERI)

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Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

The complete report, Order No._____; Cost_____, (subject to change) will be available only from:

National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161

The EPA Project Officer, Dr. Charles H. Nauman, can be contacted at:

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U.S. Environmental Protection Agency
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