MW\Pharm version 3.50 (date 22/01/2001)

(Update of version 3.30)

Instructions:

1) Run the file MW350UPD.EXE, and unzip the content into the directory containing MW\Pharm (usually C:\APO, which is the default directory).
2) Run the batch file APO350.BAT.

To use version 3.30 again, run the batch file APO330.BAT.
To use version 3.50 again, run the batch file APO350.BAT.
The version which has been used last (either 3.30 or 3.50) can be started normally with APO.BAT.

Note: Patient and drug data stored with version 3.50 are compatible with version 3.30, except for the correlations between drug parameters (stored in GEN330.DTC). If a drug is loaded for which correlations have been stored in version 3.30, the correlations database (GEN330.DTC) is updated. The old correlations database is renamed to GEN330o.DTC. If correlations are stored or imported while running version 3.50, these data cannot be accessed by version 3.30, and vice versa. Other data are not affected by the conversion.
Version 3.50 uses patient and drug data files named 'NAW330. *' and 'GEN330. *'. These files should not be renamed to 'xxx350. *' !

Extensions:

1.1. Start-Up: The command line calling the startup program APO.BAT may be extended with a directory name as a parameter. If a directory name is added, the startup is performed from this directory. If the minimally required files are not found in this directory, they are copied from the original directory (if they are not found there, the execution stops).
This option is useful if the program is located on a network, and the users do not have rights to write in the directory where the program is located. The following situations can be created:
- If the directory in the command line refers to a directory which is private to the user (e.g., on a G: drive), each user keeps its own database.
- If the directory in the command line refers to a directory which is private to the computer system (e.g., on a C: drive), each computer keeps its own database.
- If the directory in the command line refers to a directory which is accessible (write/read access) to a group of users, all users will access the same database. This option seems appropriate for most users in practice. The consequence of a joined database is that the database may be temporarily inaccessible if an other user has opened the database. However, this will occur less frequently than in version 3.30 (see #2.1.).

The directory name can be added to the command line in the section ‘properties’ of a shortcut to APO.BAT.

1.2. ResPrint: The graphics screen can be saved as a bitmap file, for use in other programs (e.g. MS Word and PowerPoint) by the command <Ctrl><b>. The filename is 'RESPRxxx.BMP', where xxx is an automatically increasing number.
To get optimal results, the format (in pixels) of these BMP files should be identical to the original format, which is 640 pixels horizontally.

1.3. Patient screen and regular dosing screen: The **dosing date**, i.e. the date at which the patient characteristics are evaluated for the dosage regimen calculation can be chosen freely by the user in the patient screen. The patient's age, as used for the creatinine clearance, is now calculated at this dosing rate, instead of actual age. The default dosing date is the present date (as given by the computer system), similar to versions up to 3.30. If a patient record is read from the database, the dosing date is set to the date of the last line in the patient history, if present.
This change of the dosing date and corresponding age does not affect the fitting of the medication history (since the actual patient age at the time of medication is taken into account, similar to earlier version), but does affect the regular dosage regimen calculation if the dosing is different from the computer date. This implies that the dosage regimen calculation is now independent of the date of calculation, which may be advantageous for demonstration purposes.

1.4. Patient screen: the date of last saving of patient records is now stored and displayed in the patient screen (see also #1.6).

1.5. Patient screen: Patient records can be searched for, and can be shown in alphabetical order of the drug name (as an alternative to patient number, name, or date of birth). In the patient menu the field 'medication' is now editable to allow entering a drug name.

1.6. **Export and import of patient and drug records** is enabled in the patient screen and drug screen, respectively. After pressing <Ctrl>e (for export) or <Ctlr>i (for import) a menu is shown.
For convenience, these functions can be called also from the Options menu, Database Utilities (identical screens and functions).

Export:
Patient or drugs can be selected by the following criteria:
- option <4>: based on the date of the last saving of the record (for patients this date is now stored in the database, see also #1.4; since this date was not stored in older versions, this option cannot be used for selecting patient records stored with earlier versions). This option is particularly useful for updating the database of other version of MW\Pharm.
- option <5>: based on the drug name. Patients using a particular drug can be selected by entering the drug name. A trailing '*' can be used as a wildcard. This option can be used also for drug records.
- option <6>: based on a patient selection file (made within the KinPop module).

This option is not available for drug records.
- option <7>: based on a manual selection by the user, similar to the selection procedure for patients in KinPop: Patients or drugs can be selected by pressing <Space>, resulting in highlighted indication. After <Esc> the selection is stored; in contrast to KinPop, the selection file is not written to disk, and cannot be retrieved later.
The selected patients or drugs are added to an internal selection list, which can be viewed and edited by option <7> and cleared by option <3>.
After entering a filename (option <1>; default filename is NAWTEMP for patients and GENTEMP for drugs) and a path (option <2>; default is A:, assuming data transfer by diskette) for the exported patient records, the data can be exported.

Import:
After entering a filename and a path for the datafile containing the records to be imported, the data can be imported. If 'interactive' import is chosen (default setting), the user can indicate for each record whether it should be imported or not. Relevant data are shown on the screen. There are 3 possibilities, indicated on the screen with different colors and symbols:
= : an identical record is present in the database; the record is not imported.
? : a record with the same keys (patient number, name, birth date and drug for patient records and drug name for drugs), but different data, is found in the database. The user can choose: 0 = do not import into database; 1 = replace record in existing database by imported record (overwriting existing data); 2 = add record as a new record in the database. Please note that this implies that duplicate records are present in the database. Both duplicates can be assessed from the selection windows in the patient or drug screen. However, KinPop will see only a single record, which may lead to unpredictable results.
: there is no record in the existing database with the same keys. The user can choose: 0 = do not import, or 1 = 2 = add record as a new record in the database.

1.7. For the extravascular routes of administration (oral and im) a **lag-time** (indicated as 'Tlag') can be included, both for the regular dosage regimen calculation and the medication history and (Bayesian) fitting.
The lag-time is stored with the drug data, and, after fitting, with the patient data, similar to the procedure for 'ka' and 'F'. The default for a missing value is zero.
After fitting of extravascular data in KinFit, the lag-time is transferred to the main program similar to the procedure for 'ka' and 'F'.

1.8. Export of confidence intervals in medication history (option 5 main menu): In case the confidence intervals of the initial (before fitting) or fitted (after fitting) concentration curve are shown on the screen (after pressing 'i'), the confidence interval, i.e. lower and upper bounds, is also exported (after pressing 'e').

1.9. Medication history (option 5 main menu): The area under the concentration - time curve (**AUC**) is now displayed in the window in the right upper corner (activated by arrow keys, <PgUp>, <PgDn>, or <F6>). In case of a changing body weight or creatinine clearance, the default setting displays LBMc and CLcr, and their graphs are shown in the upper panel; after pressing 'g' the graph disappears and AUC is

shown in the right upper corner.
AUC is the AUC from time zero to the indicated time point.
AUCi is the AUC from the time of the last dose to the indicated time point. This option allows the determination of AUC over a single interval.
Note: AUC is obtained by the trapezoidal rule on the displayed plasma concentration - time values. Therefore the calculation of AUC becomes less accurate with increasing number of doses.

1.10. KinPop: The parameter(s) describing the **assay error** can be estimated during the population analysis. When starting the KinPop procedure, a new screen is shown, allowing a change of the initial assay error parameters (constants of the polynomial function relating standard deviation to plasma concentration); in addition, the parameters can be set to 'fixed' or 'variable'. In the latter case, their value is estimated during the population analysis. If there is more than one variable parameter, their values cannot be estimated independently; KinPop keeps their ratio constant during the optimization process. Therefore the final estimates are dependent on the initial values.
If one or more of the assay error parameters is variable, the graphical presentations are extended with:
(a) the value of the assay error parameter (denoted 'sd(res)') against the cycle number.
(b) the value of the quantity 'Σ(WSS)/(Σ(N)-P)' against the cycle number. This value moves to 1 during the population analysis.

> NOTE: It is likely that the assay error parameters as determined by this procedure are significantly higher than the values obtained from the assay validation. The latter refers to the 'pure' assay error; the former to the total of the residual error, including assay error, sampling errors, model misspecification, and any other deviation from the assumptions. Therefore it seems to be more appropriate to be used in Bayesian analysis, since it is not realistic to assume that any deviation from the expected concentration is due to assay error.

1.11. KinPop: Patient selection in the KinPop menu, after choosing '1' (make patient selection file), can now be performed from a list in alphabetical order of drug name, patient number, name, or date of birth (in version 3.30 the order was determined by patient number). If an earlier saved patient selection is used, the cursor moves automatically to the first patient in the list.
If an existing patient selection file has been chosen, a warning against overwriting the existing file is given after leaving the selection box.

1.12. KinPop: After performing the KinPop analysis, after the results, the **individual graphs** of the fit of each subject are shown, one after another by <F10> or <Space> (note: <Enter> shows the graph menu, which is still active; <F1> returns to KinPop menu).
Since the initial parameters are set equal to the population parameters (as always during the population analysis), the yellow (initial) curve represents the plasma concentration profiles based on the population parameters, the light blue curve

shows the profiles for the best fitting individual parameters.
This new option is a convenient tool to evaluate the appropriate fitting in the individual patients, which is indispensable in population analysis.

1.13. KinFit: **Noncompartmental analysis** has been added to the KinFit procedure; in addition to 1-, 2-, and 3-compartment models can be chosen for a noncompartmental analysis.
AUC and AUMC (area under the C.t curve) are calculated directly from the data points by the trapezoidal rule (see also #1.14). The concentration profile after the last measured concentration is extrapolated to infinity using the terminal elimination rate constant k. k is estimated from the terminal data points. An automatic procedure selects the data points for the calculation of k: the last 3, 4, 5, et cetera data points are tested, and the number yielding the lowest residual standard deviation is selected.
Alternatively, the user can enter manually the first and last data point to be used for the calculation of k.
From AUC and AUMC the following pharmacokinetic parameters are calculated:
CL = F * Dose / AUC
V = CL / k
Vss = CL * MRT
t½ = ln(2) / k
MRT = AUMC / AUC - MIT
where MIT is the Mean Input Time. In case of intravenous bolus administration, MIT = 0, and in case of infusion MIT = T_inf / 2. In case of extravascular dosing, MIT cannot be calculated noncompartmentally, and thus MRT and Vss cannot be calculated.

1.14. KinFit: **AUC** is now calculated by the linear and logarithmic trapezoidal rule, according to the SSD criterion (Proost JH. Wagner's exact Loo-Riegelman equation: the need for a criterion to choose between the linear and logarithmic trapezoidal rule. J Pharm Sci 1985;74:793-794).
In case of intravenous bolus dosing, the concentration profile before the first measurement is obtained by back-extrapolation from the first and second measurement.
Both new methods can be optionally replaced by the procedures in the older versions of MW\Pharm (linear trapezoidal rule, and AUC calculated from origin 0,0).

1.15. KinFit: For extravascular dosing, KinFit can optionally be performed with the initial estimate of the absorption rate constant smaller than that of the fastest rate constant, the so-called **'flip-flop'** situation (the corresponding intercept values are converted automatically). Usually, the final estimate of the absorption will also be smaller than that of the fastest rate constant (exponential coefficient).

> NOTE: For any extravascular model with first-order drug absorption, TWO solutions can be found. As it is generally assumed that absorption is relative fast, the solution with the highest possible value is usually presented as 'the' solution. This is not warranted without further information.
> The 'normal' solution and the 'flip-flop' solution are mathematically equivalent.

Both solutions produce exactly the same polyexponential equation.
It may also be noticed that a polyexponential equation with one or more negative intercepts (Ce1, etc) does not necessarily represent a meaningful pharmacokinetic model. It represents a meaningful model only if all values C1, etc. are positive, as is the case after intravenous administration.

1.16. KinFit: The dose, route of administration and duration of infusion are now stored with the data in the xxx.MWF file (see also #3.21).
Note: bioavailability is not stored in the xxx.MWF file since it is not considered as a known variable (such as dose and measurements) but as a parameter (such as absorption rate constant). Since it cannot be assessed from the data, it must be entered by the user. The default value is the current parameter value for the current drug.

Corrections:

2.1. The database is now better suited for working within a network environment (in version 3.30 the performance during multiple use could be rather bad). Also, if the database is used by other users, it is now possible to quit the call to the database by pressing <F1>.

2.2. Reconstruction of database is now performed correctly in case of the option 'Make new index' (in version 3.30 deleted records were unerased, similar to the action after 'Make new index and unerase deleted records').

2.3. Patient selection screen: a bug in the function of the keys <PgDn> and <PgUp> has been solved (in older versions these functions did not work correctly in case of a large number of records with equal patient numbers or names).

2.4. The correction factor 0.9 for women in the creatinine clearance calculated by method Jelliffe II has been modified (versions up to 3.30 applied the correction factor to the total equation, instead of application to the creatinine production only); the resulting creatinine clearance is slightly different.

Note: The equations for the Jelliffe 2 have been misprinted in the manual of MW\Pharm version 3.15, Volume 3, Methods, page 9:
- The symbol ΔCr in F_1 and in F_3 should be replace by $(Cr_1 + Cr_2)/88.5$, instead of $(Cr_1 - Cr_2)/88.5$
- The symbol ΔCr in F_2 should be replace by $(Cr_2 - Cr_1)/88.5$, instead of $(Cr_1 - Cr_2)/88.5$
(Cr_2 refers to the last creatinine measurement, Cr_1 to the previous measurement).

2.5. Regular dosing screen: After recalculation of a dosage regimen after fitting, the highlighting of the practical dose is now cleared correctly.

2.6. Regular dosing screen: in case of Michaelis-Menten kinetics, the values of

Cmax and Cmin are now calculated correctly if the number of doses exceeds 10 (in earlier versions the values were approximations; only in case of multi-compartment kinetics the differences may be significant; graphics were correct in earlier versions).

2.7. Regular dosing screen: after pressing <F4>, the original dosing schedule is saved, and is retrieved automatically after repeated <F4> (in version 3.30 it was lost).

2.8: Graphics: in case of molar concentration units, the representation on the Y-axis is now corrected (in version 3.30 values along the Y-axis could be incorrect).

2.9: Medication history (option 5 main menu): In case of very small values for dose, concentration, et cetera, the value is now printed in exponential notation on the screen (in versions up to 3.30, these values were printed in exponential notation, without the exponent).

2.10. Medication history (option 5 main menu): The calculation of the creatinine clearance in case of extracorporeal clearance has been modified drastically.
The effect on extracorporeal clearance is now calculated more accurately, by taking into account the time at which it occurs. The effect of extracorporeal clearance, and thus of the calculated creatinine clearance, wears off with time. Eventually, the creatinine level will return to the same steady-state concentration, irrespective of the earlier occurrence of extracorporeal clearance.
The effect of extracorporeal clearance on the creatinine level is now shown in the upper panel: during extracorporeal clearance, the creatinine level is decreasing rapidly, whereas after stopping the extracorporeal clearance the creatinine level increases slowly to a steady-state level.

2.11. Medication history (option 5 of main menu): Correction of bug in case of 'flip-flop' kinetics, i.e. if the absorption rate constant is smaller than the elimination rate constant (in version 3.30 this situation gave erroneous results, if only one body weight and one creatinine level were given).

2.12. Medication history (option 5 of main menu): Correction of bug in case that the unit of dose is not 'mg' or the unit of concentration is not 'mg/l' (in version 3.30, these cases were not handled correctly for Km and Vmax).

2.13. Medication history (option 5 main menu): An error in the indication of dates on the X-axis has been corrected (in version 3.30 the indication was erroneous in some exceptional cases).

2.14. Medication history (option 5 main menu): The graphical presentation in case of a very large number of doses (typically, 200 or more) is improved by plotting both the minimum and maximum concentration after each dose (in earlier versions, the maximum concentration was always plotted correctly, but the minimum concentration was sometimes 'missed').

2.15. Medication history (option 5 main menu): In the following situations, version 3.30 gave erroneous results during fitting of the medication history, if BOTH of the following conditions met:
- one or more SD values (SD of population parameters or assay error) were missing (i.e., if weighting 'OFF' in fitting menu);
- after changing 'calculation of CL or kel' from 'kel = kelm + kelr * CLcr' to 'CL = CLm * BSA/1.85 + fr * CLcr'.

2.16. Medication history (option 5 of main menu): After fitting data in the medication history screen with non-zero values at time zero for the concentration (c(0)) or amount to be absorbed (d(0)_po or d(0)_im), the values of c(0), d(0)_po and d(0)_im are correctly saved between calculations (in versions 3.30 these values could be changed).

2.17. Medication history (option 5 of main menu): After fitting extravascular data in the medication history screen, printing the results by <Ctrl>P is performed correctly (in versions 3.30 the program could be aborted by an 'illegal function call').

2.18. KinPop: Correction of bugs in case that the unit of dose is not 'mg' or the unit of concentration is not 'mg/l' (in version 3.30, these cases were not handled correctly in KinPop).

2.19. KinPop: After choosing '1' and entering a filename of an existing patient selection file, the patients in that file remain in the selection, as indicated by highlighting. In version 3.30 the selection was cleared.

2.20. KinPop: After population analysis with Bayes OFF (results in Standard Two-Stage analysis), the plot of the quantity 'ΣWSS/(ΣN-P)' (denominator is the degrees of freedom, the total number of measurements minus the number of population parameters) is now replaced by 'ΣWSS/Σ(N-P)' (denominator is the degrees of freedom, the sum of the degrees of freedom for each patient), since this quantity moves to 1 during the analysis if Bayes is OFF (the value in version 3.30 was meaningless).

2.21. KinPop: KinPop works now correct also in case of more than 8 parameters (in version 3.30 a runtime error occurred).

2.22. KinPop: Non-relevant parameters (e.g. ka and F in case of intravascular dosing) are not shown anymore.

2.23. KinFit: A bug in version 3.30 with respect to the transfer of the parameters V2 and V3 to the main program has been fixed (for one-compartment kinetics, and if the kinetic model in the medication is set 'k12 & k21', which is the default value, the transfer in these versions was correct).
In addition, all transferred parameters are now shown on the screen.

2.24. KinFit: After entering an incorrect selection criterion for files to be shown, the program continues normally (in version 3.30 the program jumped to the KinFit

menu).

2.25. KinFit: In cases where the standard error of a parameter cannot be calculated, this is indicated by '###' instead of a value 0.

2.26. KinFit: Printing procedure in KinFit has been improved (earlier versions caused problems in some cases).

2.27. KinFit, HPstrip: In case of a long-lasting infusion, a math overflow in the calculated intercepts of HPstrip could occur. To avoid this error, intercepts now refer to their value at the time where infusion stops.

Other changes:

3.1. In the start-up batchfile APO.BAT, the 'code page' is set to 437. In many systems the default code page is 850, which results in some deviating characters on the screen, e.g. in the edges of frame of the regular dosing screen, and for the symbol 'Σ' in KinPop. If you still get these deviating characters, it is most likely that the file 'EGA.CPI' cannot be found. In that case you have to find the location of this file, and modify in the file APO.BAT the path to this file, in line 12 of APO.BAT.

3.2. Patient screen: existing data can now be edited, including date or birth (and dosing date; see #1.3) in case of mistyping. The existing data line can be deleted by <Esc>, or by repeated <BS>.

3.3. Patient selection screen (in KinPop and in patient menu): A new function <Ctrl><DownArrow> (^↓) and <Ctrl><UpArrow> (^↑) has been added.
<Ctrl><DownArrow> moves the cursor down, and copies the 'status' of the previous record to the new record; in KinPop, the 'status' is: 'highlighted' = selected, 'normal' is not selected. In the patient menu: 'grey' = 'marked deleted', and 'normal' is not marked.
This function allows a fast selection of a list of patient records.

3.4. Patient screen and mediation screen: records of a patient or a drug can be deleted directly from the list in the open window, by pressing <Ctrl><Del> when the patient or drug is indicated by the green bar. The color of the deleted record turns to darkgrey. The record can be undeleted by pressing <Ctrl><Ins>. This can be done until the window has been left by <Enter>, <Esc>, <F1> or <F10>.

3.5. Medication screen: filling an 'individual' value automatically fills the corresponding 'population' value if it is missing, and vice versa.

3.6. Medication screen: All drug data can be cleared by <Ctrl><s> in the medication screen. Also, all drug data are cleared after selecting the standard patient by <Ctrl><s> in the patient menu.

3.7. Medication screen: Using the 'growth/kill' PK/PD model, the parameter zMIC

can now be entered directly, and EC50 is calculated automatically and shown.

3.8. Metabolite kinetics: Metabolites with multicompartment kinetics based on clearance model are now allowed. In earlier versions a message 'Metabolite data in drug data missing' was shown.

3.9. Medication history (option 5 of main menu): If case of fitting with unknown initial plasma concentration, i.e. c(0) > 0, and/or unknown earlier extravascular doses, i.e. d(0) > 0, the standard error of the estimated values are now given.

3.10. Medication history (option 5 main menu): During export of the curves (by pressing 'e') the curves of the creatinine clearance and LBMc are exported only if they are shown on the screen (by pressing 'g').

3.11. Medication history (option 5 main menu): The ability to read data from xxx.MWF files (made by KinFit or from other sources) has been extended. Files made by Windows programs, e.g. Excel or Word can now be read with less restrictions. E.g., TABs can be used as delimiters.
The general format is:
- first line: number of time - concentration data pairs
- second line: first data pair, time and concentration, separated by one or more spaces (or TABs).
- third line: second data pair, et cetera.
In addition, the file format of the program MultiFit can be read, including units, multiple dosing and 'unused' marks.
If the unit of dose starts with 'u', this is interpreted as 'µ'.
If the unit of dose includes '/kg', the dose is converted using the current patient's body weight.
If the unit of time start with 'min', the time values are converted to hours.

3.12. KinPop: after leaving the patient selection screen, a warning is given for overwriting an existing selection file (e.g. in case of a mistake, the existing selection file is not modified after entering 'N').

3.13. KinPop: calculation can be started by pressing <F10> (similar action as choosing '9' from menu).

3.14. KinPop: during the screens showing the initial assay error parameters and kinetic parameter, pressing <F1> returns to the KinPop menu.

3.15. KinPop: The order of presentation of the graphs is modified; first, the graphs of the various quantities against the cycle number are shown, followed by the distribution and correlation plots of the individual parameters.

3.16. KinPop: The quantity 'ΣWSS/(ΣN-P)' (if Bayes ON) or 'ΣWSS/Σ(N-P)' (if Bayes OFF) is now also shown on the results screen. The plot of this quantity against the cycle number is now also shown for fixed assay error parameters.
This quantity is also saved in the results file, instead of the quantity ΣWSS (version

3.30).

> NOTE: If the assay error parameters are fixed, this quantity do not converge to 1. Its final value is a measure for the order of magnitude of the residuals relative to the assumed assay error. A value not too far from 1 (say, between 0.5 and 2) indicates that the assumed assay error is consistent with the observed residuals; a lower value indicates that the actual residuals are smaller than expected from the assumed assay error (a rather exceptional case); a higher value indicates that the actual residuals are larger than expected from the assumed assay error (a more common case).

3.17. KinPop: The occurrence of extravascular dosing (oral or intramuscular, or both) in the medication history in selected patients is detected and the presence of the required population parameters is checked before the analysis starts. In earlier versions extravascular dosing was detected and taken into account only if it occurred in medication history of the first patient.

3.18. KinPop: Result files are not overwritten if indicated by the user. In earlier versions these files were overwritten in spite of answering 'N'.

3.19. KinPop: During generating Monte Carlo simulation sets (option 5 in main menu) some corrections are made automatically in order to prevent unrealistic data:
- Randomly simulated individual parameters with a value less than 1% of that of the population parameter are corrected to 1% of that of the population parameter. This avoids extremely small, zero or negative parameters.
- Randomly simulated measurements with a value less than 1% of the noise-free value are corrected to 1% of the noise-free value. This avoids extremely small, zero or negative measurements due to random noise (Note: noise-free concentration value may still be very small; a minimum concentration value can be entered by the user).
- In case of log-normally distributed assay errors and a non-zero constant assay error term (S0), the randomly simulated measurements with a value more than 100 time the noise-free value are corrected to 100 times the noise-free value. This avoids extremely large measurement errors due to random noise.

The aforementioned conditions produce extreme and unrealistic data, which may cause computational problems. It is unlikely that the corrections affect the performance of the Monte Carlo significantly.

3.20. KinPop: During Monte Carlo analysis of more than one set simultaneously, a report file on the 'true' parameters is generated. It has the same format as the report file of the calculated parameters, with extension 'MCT' ('Monte Carlo True') instead of 'MCP' (Monte Carlo Parameters'). This report allows a more convenient comparison of the MCP results than a comparison to the 'exact' values.
Each row contains the following data:
- set number
- mean values of ‘true’ individual parameters
- standard deviations of ‘true’ individual parameters
- correlations between ‘true’ individual parameters

- root mean squared error of measurements (deviation of measurement from ‘true’ value divided by ‘true’ value); in case of a proportional assay error (using S1, wih S0 = S2 = S3 = 0) this value is comparable to the corresponding value in the MCP file.
- root mean squared error of parameters (deviation of individual parameter from ‘true’ value divided by ‘true’ value); this value is measure of the typical error in the inidividual parameters, and is not comparable to the corresponding value in the MCP file.
- mean value of weighted sum of squares of weighted residuals of measurements (deviation from ‘true’ values divided by assay error as defined in medication screen) divided by the number of measurements (ΣWSS/ΣN); the expected value is 1.
- value 1 (in MCP-files: number of cycles).

3.21. KinFit: The KinFit menu now includes the route of administration, dose, infusion time (if applicable), and bioavailability (if applicable). These data can be entered after leaving the editor screen by <F10>, or by pressing <Shift>(1> in the KinFit menu. In case of missing data, the program asks for the missing data before performing HPstrip or KinFit.

3.22. KinFit: In case of multicompartment kinetics, the parameters CL12 and V2 (and CL13 and V3 in case of 3-compartment kinetics) have been added to the parameter list, according to the following relationships:

CL12 = k12 * V1	V2 = V1 * k12 / k21
CL13 = k13 * V1	V3 = V1 * k13 / k31

3.23. KinFit: The ability to read data from xxx.MWF (from sources other than KinFit) files has been extended. See #3.11. Multiple dosing and 'unused' marks are not supported in KinFit.

3.24. Option menu: Patient records can now be printed in alphabetical order of the drug name.

3.25. Option menu: Resolution of graphical presentation can be changed in calculation option menu. The default value of 600 is suited for most purposes (corresponding to the resolution of a VGA screen). A higher value may be advantageous in case of a large number of doses (better peak and trough presentation), or in case of zooming graphics by the 'z' command.