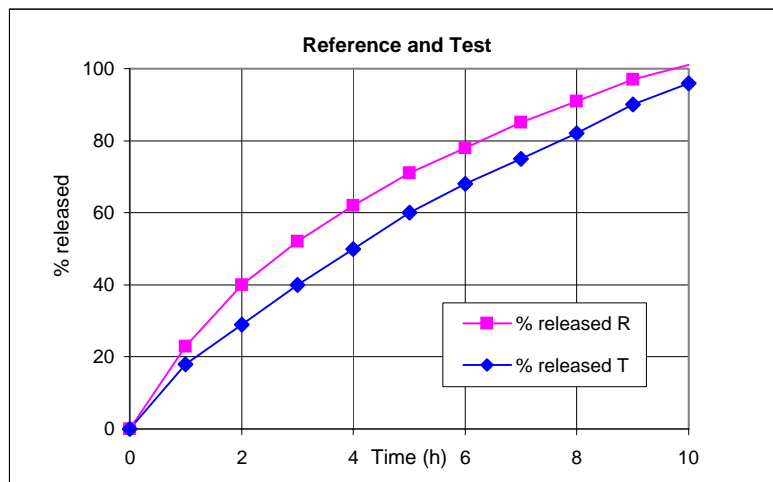


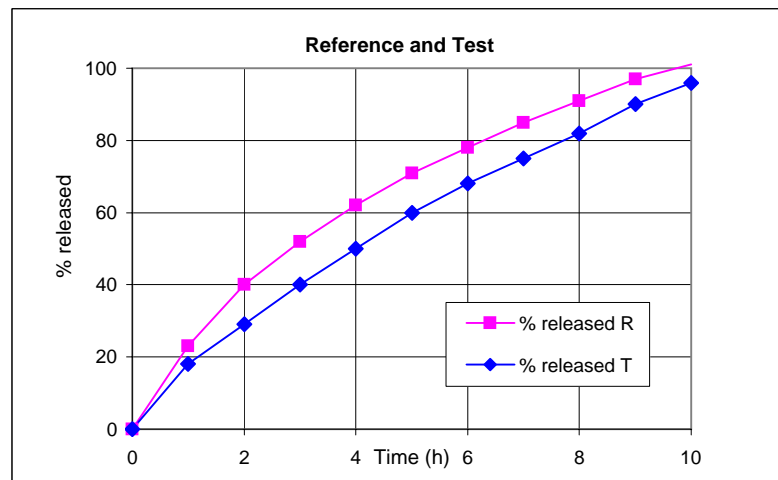
F1, F2 comparison: Example 1

| Time | % released R | % released T | R-T |
|------|--------------|--------------|-----|
| 0 | 0 | 0 | 0 |
| 1 | 23 | 18 | 5 |
| 2 | 40 | 29 | 11 |
| 3 | 52 | 40 | 12 |
| 4 | 62 | 50 | 12 |
| 5 | 71 | 60 | 11 |
| 6 | 78 | 68 | 10 |
| 7 | 85 | 75 | 10 |
| 8 | 91 | 82 | 9 |
| 9 | 97 | 90 | 7 |
| 10 | 101 | 96 | 5 |



| obs | Time | % released R | % released T | R-T | (R-T) ² |
|-------|------|--------------|--------------|-------|--------------------|
| 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 1 | 23 | 18 | 5 | 25 |
| 2 | 2 | 40 | 29 | 11 | 121 |
| 3 | 3 | 52 | 40 | 12 | 144 |
| 4 | 4 | 62 | 50 | 12 | 144 |
| 5 | 5 | 71 | 60 | 11 | 121 |
| 6 | 6 | 78 | 68 | 10 | 100 |
| 7 | 7 | 85 | 75 | 10 | 100 |
| 8 | 8 | 91 | 82 | 9 | 81 |
| 9 | 9 | 97 | 90 | 7 | 49 |
| 10 | 10 | 101 | 96 | 5 | 25 |
| <hr/> | | <hr/> | | <hr/> | |
| 7 | | 411 | | 71 | 755 |

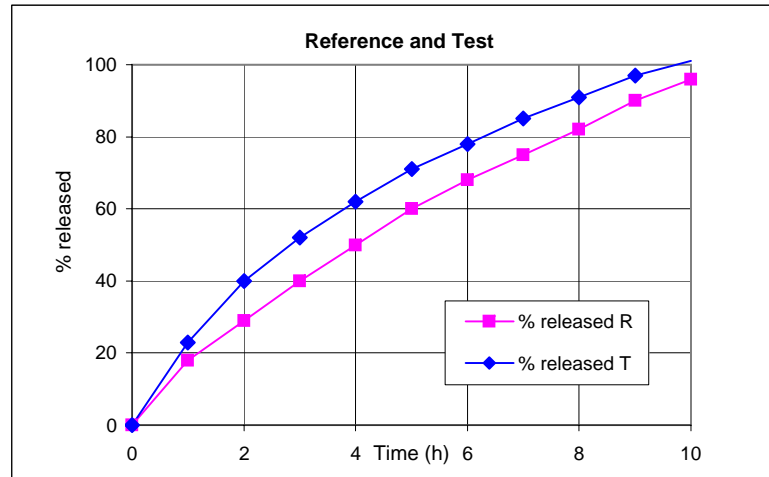
Difference factor f1: **17.27**
 Similarity factor f2: **49.08**



Remarks:
 only values up to and including 7 hrs to be used / 85%

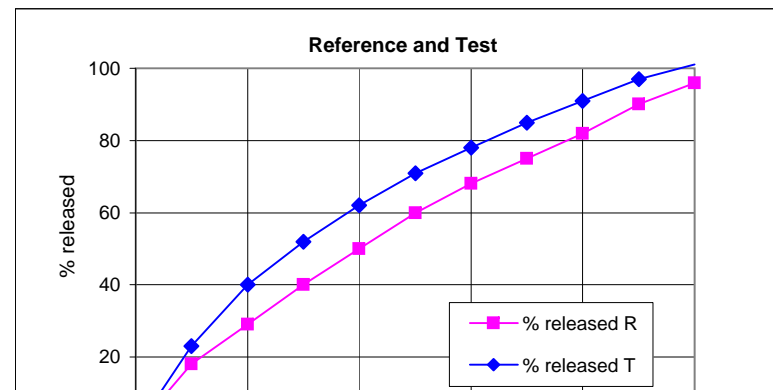
F1, F2 comparison: Example 2

| Time | % released R | % released T | R-T |
|------|--------------|--------------|-----|
| 0 | 0 | 0 | 0 |
| 1 | 18 | 23 | 5 |
| 2 | 29 | 40 | 11 |
| 3 | 40 | 52 | 12 |
| 4 | 50 | 62 | 12 |
| 5 | 60 | 71 | 11 |
| 6 | 68 | 78 | 10 |
| 7 | 75 | 85 | 10 |
| 8 | 82 | 91 | 9 |
| 9 | 90 | 97 | 7 |
| 10 | 96 | 101 | 5 |



F1, F2 comparison: Example 2

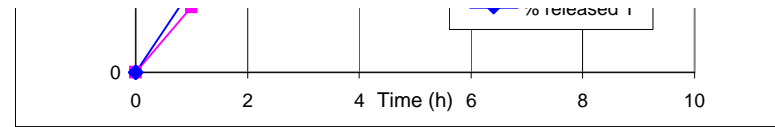
| Time | % released R | % released T | R-T | (R-T) ² |
|------|--------------|--------------|-----|--------------------|
| 0 | 0 | 0 | 0 | 0 |
| 1 | 18 | 23 | 5 | 25 |
| 2 | 29 | 40 | 11 | 121 |
| 3 | 40 | 52 | 12 | 144 |
| 4 | 50 | 62 | 12 | 144 |
| 5 | 60 | 71 | 11 | 121 |
| 6 | 68 | 78 | 10 | 100 |
| 7 | 75 | 85 | 10 | 100 |
| 8 | 82 | 91 | 9 | 81 |
| 9 | 90 | 97 | 7 | 49 |
| 10 | 96 | 101 | 5 | 25 |
| 340 | | 71 755 | | |



Example 2

demo f2 comparisons.xls

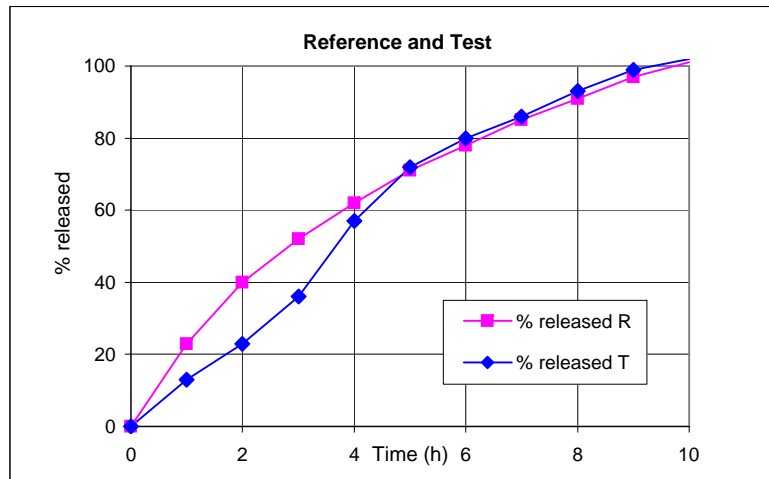
Difference factor f1: 20.88
Similarity factor f2: 49.08



Remarks:
note the difference in f1 after exchanging R and T

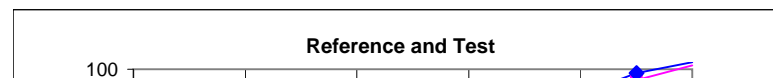
F1, F2 comparison: Example 3

| Time | % released R | % released T | R-T |
|------|--------------|--------------|-----|
| 0 | 0 | 0 | 0 |
| 1 | 23 | 13 | 10 |
| 2 | 40 | 23 | 17 |
| 3 | 52 | 36 | 16 |
| 4 | 62 | 57 | 5 |
| 5 | 71 | 72 | 1 |
| 6 | 78 | 80 | 2 |
| 7 | 85 | 86 | 1 |
| 8 | 91 | 93 | 2 |
| 9 | 97 | 99 | 2 |
| 10 | 101 | 102 | 1 |



F1, F2 comparison: Example 3

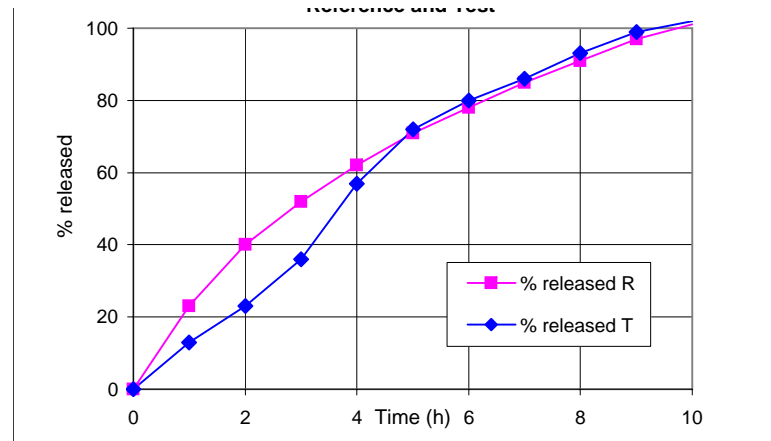
| obs | Time | % released R | % released T | R-T | (R-T) ² |
|-----|------|--------------|--------------|-----|--------------------|
| 0 | 0 | 0 | 0 | 0 | 0 |



demo f2 comparisons.xls

| | | | | | |
|-------|----|-----|-----|----|-----|
| 1 | 1 | 23 | 13 | 10 | 100 |
| 2 | 2 | 40 | 23 | 17 | 289 |
| 3 | 3 | 52 | 36 | 16 | 256 |
| 4 | 4 | 62 | 57 | 5 | 25 |
| 5 | 5 | 71 | 72 | 1 | 1 |
| 6 | 6 | 78 | 80 | 2 | 4 |
| 7 | 7 | 85 | 86 | 1 | 1 |
| 8 | 8 | 91 | 93 | 2 | 4 |
| 9 | 9 | 97 | 99 | 2 | 4 |
| 10 | 10 | 101 | 102 | 1 | 1 |
| <hr/> | | | | | |
| 7 | | 411 | | 52 | 676 |

Difference factor f1: **12.65**
 Similarity factor f2: **50.27**

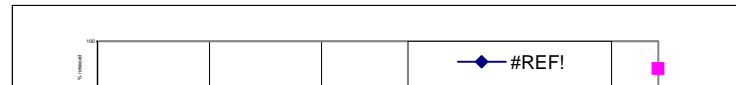


Remarks:

although f1 and f2 suggest similarity, the comparison is not suitable because the profiles suggest different release kinetics

10 101 91
Difference factor, f1: **16.95**
Similarity factor, f2: **49.89**
Rescigno index: **0.089**

| Time | %rel R 4 | % rel T4 |
|------|----------|----------|
| 0 | 0 | 0 |
| 1 | 23 | 0 |
| 2 | 40 | 23 |
| 3 | 52 | 40 |



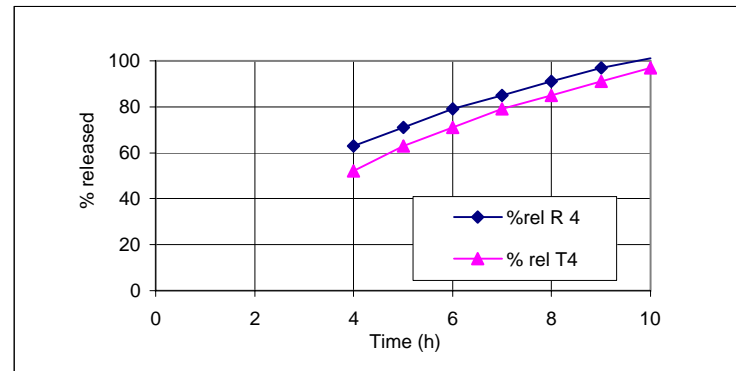
demo f2 comparisons.xls

Example 3

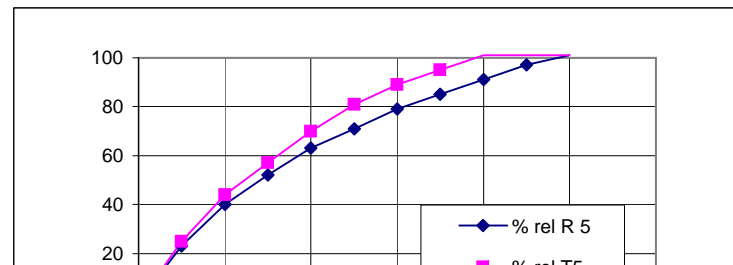
demo f2 comparisons.xls

| | | |
|----|-----|----|
| 4 | 63 | 52 |
| 5 | 71 | 63 |
| 6 | 79 | 71 |
| 7 | 85 | 79 |
| 8 | 91 | 85 |
| 9 | 97 | 91 |
| 10 | 101 | 97 |

Difference factor, f1: **20.58**
 Similarity factor, f2: **43.67**
 Rescigno index: **0.127**



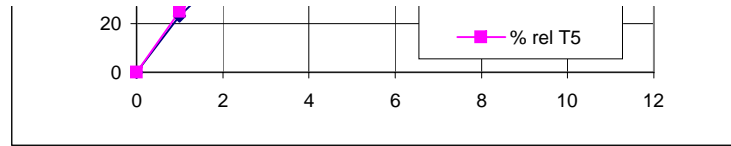
| Time | % rel R 5 | % rel T5 |
|------|-----------|----------|
| 0 | 0 | 0 |
| 1 | 23 | 25 |
| 2 | 40 | 44 |
| 3 | 52 | 57 |
| 4 | 63 | 70 |
| 5 | 71 | 81 |
| 6 | 79 | 89 |
| 7 | 85 | 95 |



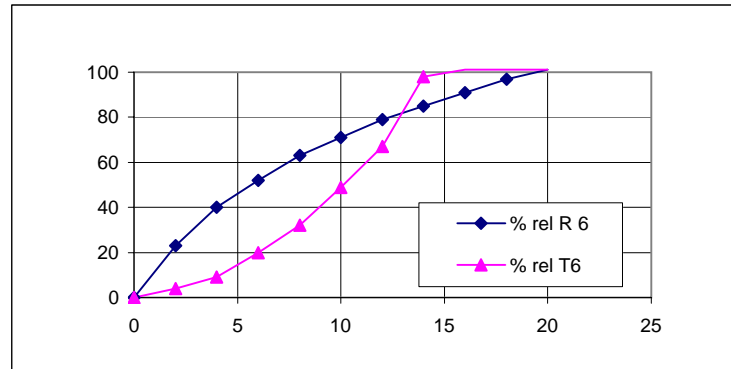
Example 3

demo f2 comparisons.xls

| | | |
|------------------------|-----|--------------|
| 8 | 91 | 101 |
| 9 | 97 | 101 |
| 10 | 101 | 101 |
| Difference factor, f1: | | 11.59 |
| Similarity factor, f2: | | 57.53 |
| Rescigno index: | | 0.053 |

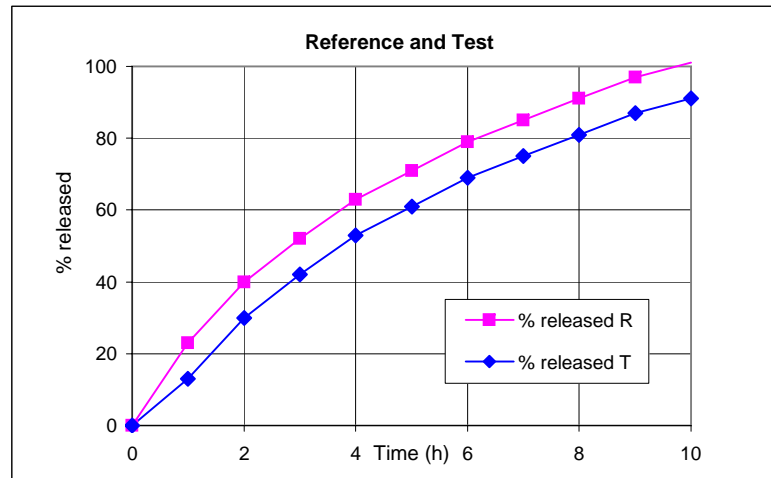


| time (min) | % rel R 6 | % rel T6 |
|------------------------|-----------|--------------|
| 0 | 0 | 0 |
| 2 | 23 | 4 |
| 4 | 40 | 9 |
| 6 | 52 | 20 |
| 8 | 63 | 32 |
| 10 | 71 | 49 |
| 12 | 79 | 67 |
| 14 | 85 | 98 |
| 16 | 91 | 101 |
| 18 | 97 | 101 |
| 20 | 101 | 101 |
| Difference factor, f1: | | 38.7 |
| Similarity factor, f2: | | 30.8 |
| Rescigno index: | | 0.225 |



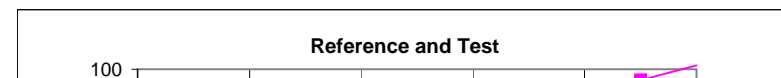
F1, F2 comparison: Example 5

| Time | % released R | % released T | R-T |
|------|--------------|--------------|-----|
| 0 | 0 | 0 | 0 |
| 1 | 23 | 13 | 10 |
| 2 | 40 | 30 | 10 |
| 3 | 52 | 42 | 10 |
| 4 | 63 | 53 | 10 |
| 5 | 71 | 61 | 10 |
| 6 | 79 | 69 | 10 |
| 7 | 85 | 75 | 10 |
| 8 | 91 | 81 | 10 |
| 9 | 97 | 87 | 10 |
| 10 | 101 | 91 | 10 |



F1, F2 comparison: Example 4

| obs | Time | % released R | % released T | R-T | (R-T) ² |
|-----|------|--------------|--------------|-----|--------------------|
| 0 | 0 | 0 | 0 | 0 | 0 |

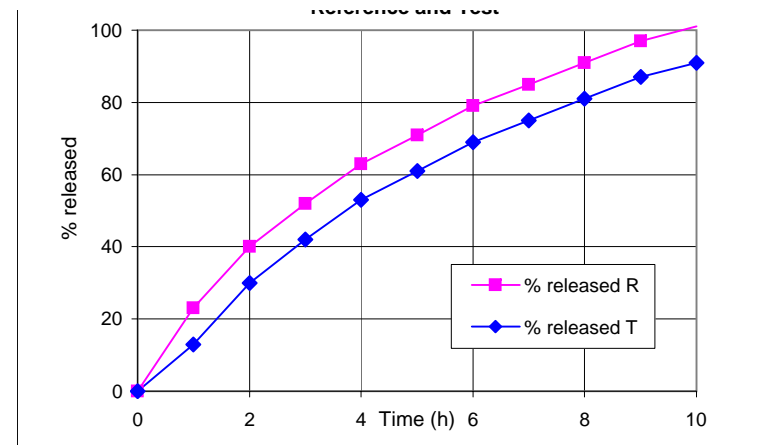


Example 4

demo f2 comparisons.xls

| | | | | | |
|-------|----|-----|----|----|-----|
| 1 | 1 | 23 | 13 | 10 | 100 |
| 2 | 2 | 40 | 30 | 10 | 100 |
| 3 | 3 | 52 | 42 | 10 | 100 |
| 4 | 4 | 63 | 53 | 10 | 100 |
| 5 | 5 | 71 | 61 | 10 | 100 |
| 6 | 6 | 79 | 69 | 10 | 100 |
| 7 | 7 | 85 | 75 | 10 | 100 |
| 8 | 8 | 91 | 81 | 10 | 100 |
| 9 | 9 | 97 | 87 | 10 | 100 |
| 10 | 10 | 101 | 91 | 10 | 100 |
| <hr/> | | | | | |
| 7 | | 413 | | 70 | 700 |

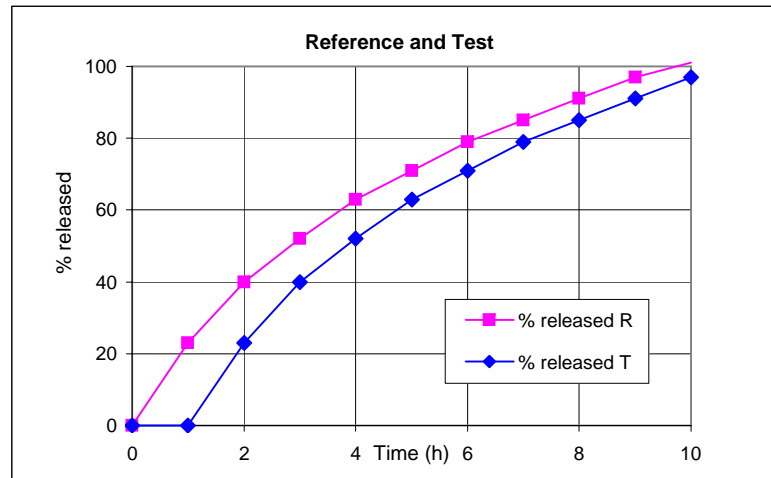
Difference factor f1: **16.95**
 Similarity factor f2: **49.89**



Remarks:
 lower extreme value for similarity (10% difference)

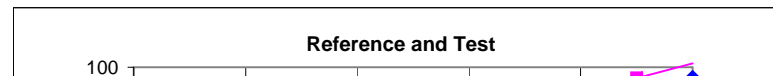
F1, F2 comparison: Example 5

| Time | % released R | % released T | R-T |
|------|--------------|--------------|-----|
| 0 | 0 | 0 | 0 |
| 1 | 23 | 0 | 23 |
| 2 | 40 | 23 | 17 |
| 3 | 52 | 40 | 12 |
| 4 | 63 | 52 | 11 |
| 5 | 71 | 63 | 8 |
| 6 | 79 | 71 | 8 |
| 7 | 85 | 79 | 6 |
| 8 | 91 | 85 | 6 |
| 9 | 97 | 91 | 6 |
| 10 | 101 | 97 | 4 |



F1, F2 comparison: Example 5

| Time | % released R | % released T | R-T | (R-T) ² |
|------|--------------|--------------|-----|--------------------|
| 0 | 0 | 0 | 0 | 0 |

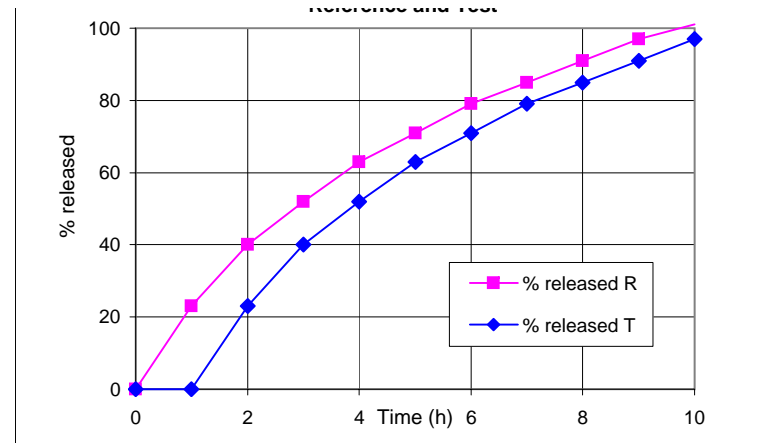


demo f2 comparisons.xls

| | | | | |
|-------|-----|----|----|------|
| 1 | 23 | 0 | 23 | 529 |
| 2 | 40 | 23 | 17 | 289 |
| 3 | 52 | 40 | 12 | 144 |
| 4 | 63 | 52 | 11 | 121 |
| 5 | 71 | 63 | 8 | 64 |
| 6 | 79 | 71 | 8 | 64 |
| 7 | 85 | 79 | 6 | 36 |
| 8 | 91 | 85 | 6 | 36 |
| 9 | 97 | 91 | 6 | 36 |
| 10 | 101 | 97 | 4 | 16 |
| <hr/> | | | | |
| | 413 | | 85 | 1247 |

Difference factor f1:
Similarity factor f2:

20.58
#REF!

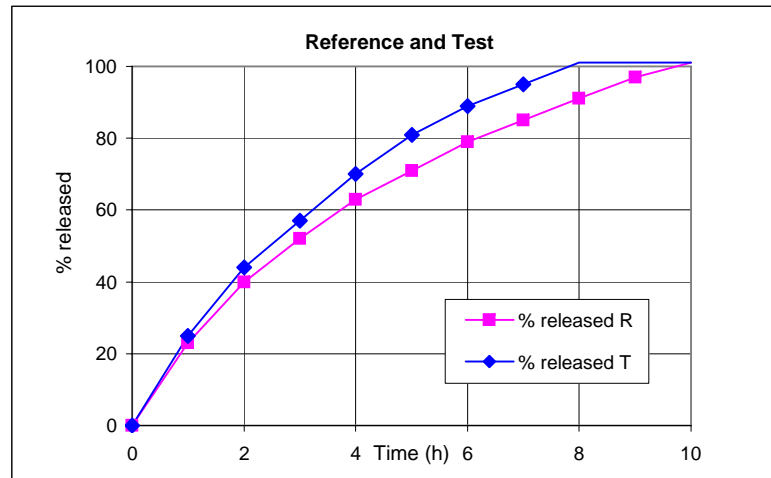


Remarks:

the test formulation was subjected to 60min pH 1.2 before the medium was switched to a buffer of 6.8

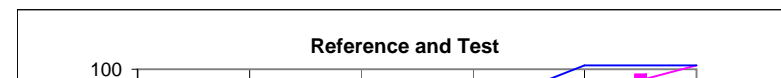
F1, F2 comparison: Example 6

| Time | % released R | % released T | R-T |
|------|--------------|--------------|-----|
| 0 | 0 | 0 | 0 |
| 1 | 23 | 25 | 2 |
| 2 | 40 | 44 | 4 |
| 3 | 52 | 57 | 5 |
| 4 | 63 | 70 | 7 |
| 5 | 71 | 81 | 10 |
| 6 | 79 | 89 | 10 |
| 7 | 85 | 95 | 10 |
| 8 | 91 | 101 | 10 |
| 9 | 97 | 101 | 4 |
| 10 | 101 | 101 | 0 |



F1, F2 comparison: Example 6

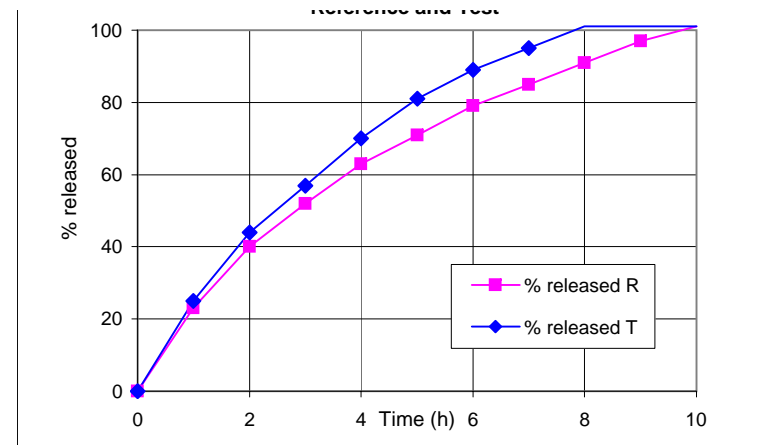
| obs | Time | % released R | % released T | R-T | (R-T) ² |
|-----|------|--------------|--------------|-----|--------------------|
| 0 | 0 | 0 | 0 | 0 | 0 |



demo f2 comparisons.xls

| | | | | | |
|-------|----|-------|-----|-------|-----|
| 1 | 1 | 23 | 25 | 2 | 4 |
| 2 | 2 | 40 | 44 | 4 | 16 |
| 3 | 3 | 52 | 57 | 5 | 25 |
| 4 | 4 | 63 | 70 | 7 | 49 |
| 5 | 5 | 71 | 81 | 10 | 100 |
| 6 | 6 | 79 | 89 | 10 | 100 |
| 7 | 7 | 85 | 95 | 10 | 100 |
| 8 | 8 | 91 | 101 | 10 | 100 |
| 9 | 9 | 97 | 101 | 4 | 16 |
| 10 | 10 | 101 | 101 | 0 | 0 |
| <hr/> | | <hr/> | | <hr/> | |
| 6 | | 328 | | 38 | 294 |

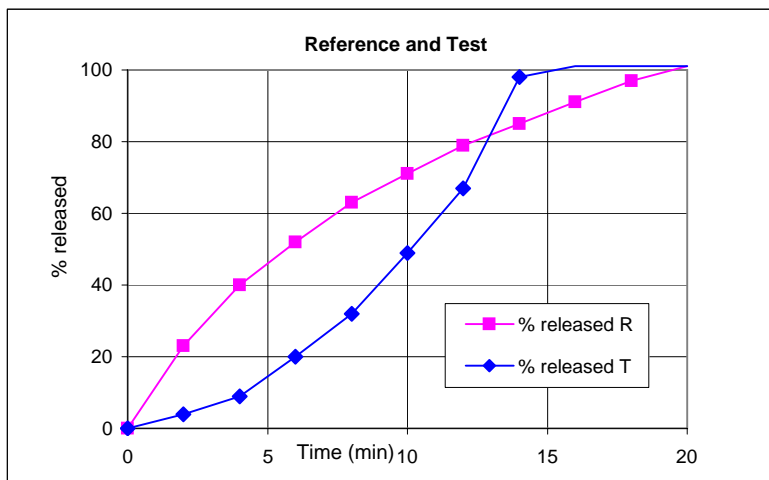
Difference factor f1: **11.59**
 Similarity factor f2: **57.53**



Remarks:
 Example for met similarity criteria

F1, F2 comparison: Example 7

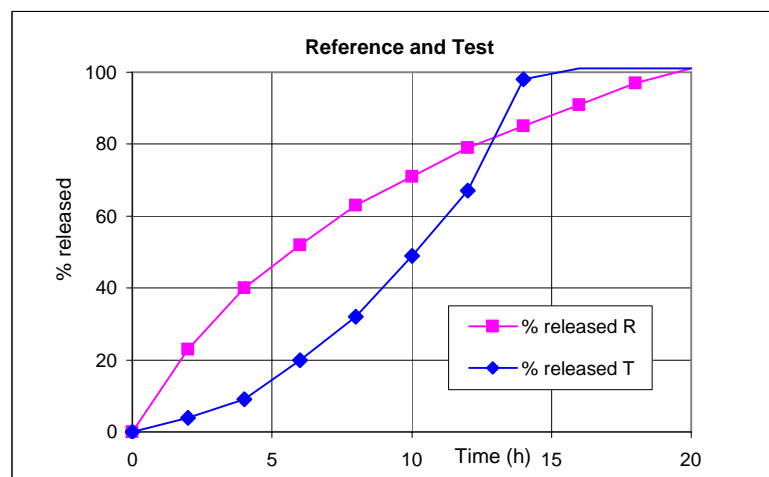
| Time | % released R | % released T | R-T |
|------|--------------|--------------|-----|
| 0 | 0 | 0 | 0 |
| 2 | 23 | 4 | 19 |
| 4 | 40 | 9 | 31 |
| 6 | 52 | 20 | 32 |
| 8 | 63 | 32 | 31 |
| 10 | 71 | 49 | 22 |
| 12 | 79 | 67 | 12 |
| 14 | 85 | 98 | 13 |
| 16 | 91 | 101 | 10 |
| 18 | 97 | 101 | 4 |
| 20 | 101 | 101 | 0 |



F1, F2 comparison: Example 7

| obs | Time | % released R | % released T | R-T | (R-T) ² |
|-------|------|--------------|--------------|-------|--------------------|
| 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 2 | 23 | 4 | 19 | 361 |
| 2 | 4 | 40 | 9 | 31 | 961 |
| 3 | 6 | 52 | 20 | 32 | 1024 |
| 4 | 8 | 63 | 32 | 31 | 961 |
| 5 | 10 | 71 | 49 | 22 | 484 |
| 6 | 12 | 79 | 67 | 12 | 144 |
| 7 | 14 | 85 | 98 | 13 | 169 |
| 8 | 16 | 91 | 101 | 10 | 100 |
| 9 | 18 | 97 | 101 | 4 | 16 |
| 10 | 20 | 101 | 101 | 0 | 0 |
| <hr/> | | <hr/> | | <hr/> | |
| 7 | | 413 | | 160 | 4104 |

Difference factor f1: 38.74
 Similarity factor f2: 30.78



Remarks:
 the similarity calculations should not be done, both formulations are immediate release forms and rapidly dissolving