

Stability studies have been carried out in accordance with the Note for Guidance on stability testing: Stability testing of existing active substances and related finished products (CPMP/QWP/122/02/Rev 1) and the Note for Guidance on declaration of storage conditions (CPMP/QWP/609/96/Rev 1).

Types of studies conducted

Six product batches have been included to the stability testing program.

Batch	Batch size	Date of manufacture	Date of storage	Container closure system
31901	275 kg	13.02.2001	08.2001	Alu-PVC blisters
32444	550 kg	22.05.2001	08.2001	Alu-PVC blisters
38359	550 kg	03.02.2004	03.2004	Alu-PVC blisters
50648	550 kg	05.11.2008	03.2009	Alu-PVC blisters
51021	550 kg	05.12.2008	03.2009	Alu-PVC blisters
51341	550 kg	29.01.2009	03.2009	Alu-PVC blisters

Composition and manufacturing process were the same as intended for marketing (module 3.2.P.1, module 3.2.P.3.3).

Packaging material

The tablets were packaged to pharmaceutical blisters with a 250 µm PVC blister base and a 20 µm thick aluminium covering film, the same as intended for transportation and use of the drug product (module 3.2.P.6).

General test methodology

Stability studies have been performed at long-term, intermediate and accelerated conditions.

Study	Storage conditions	Sampling time points
Accelerated	40 ± 2°C, 75% RH ± 5% RH ⁽¹⁾	0, 3, 6 months
Intermediate	30 ± 2°C, 65% RH ± 5% RH ⁽¹⁾	0, 3, 6, 9, 12 (18, 36) months
Long-term	25 ± 2°C, 60% RH ± 5% RH ⁽¹⁾	0, 3, 6, 9, 12, 18, 24, 36, 48, 60 months
Long-term	30 ± 2°C, 75% RH ± 5% RH ⁽²⁾	0, 3, 6, 9, 12, 18, 24, 36, 48, 60 months

⁽¹⁾ Batches 31901, 32444, 38359.

⁽²⁾ Batches 50648, 51021, 51341.

Specifications at shelf-life testing

Test	Specification SP750540-shelf-life, valid version	Procedure PA750540-shelf-life, valid version
Description	almost white, odourless film-coated tablets, round and biconvex with a snap-tab score on one side, 9 mm in diameter	organoleptic inspection
Height	3.4 – 4.1 mm	measurement
Average mass	259.6 mg ± 5% (246.6 – 272.6 mg)	weighing
Resistance to crushing	≥ 50 N	Ph. Eur. 2.9.8
Disintegration	≤ 10 min	Ph. Eur. 2.9.1
Subdivision*	complies with the test	Ph. Eur. Tablets
Dissolution		
Trospium chloride	≥ 80% after 10 min	Ph. Eur. 2.9.3, HPLC
Identification		
Trospium chloride	retention time of the principal peak is identical to that of the reference	HPLC
Related substances		
Benzilic acid	≤ 0.3%	HPLC
Unidentified, single	≤ 0.2%	HPLC
Unidentified, total	≤ 0.5%	HPLC
Total impurities	≤ 0.8%	HPLC
Microbiological quality*	complies with criteria of Ph. Eur. 5.1.4, non-aqueous prep. for oral use	Ph. Eur. 2.6.12, 2.6.13
Assay		
Trospium chloride	95.0% to 105.0% of label claim (28.5 – 31.5 mg per tablet)	HPLC

* The test is performed at least at start and at the end of shelf-life testing.

Analytical procedures

In principle, the analytical procedures have been the same as employed at release testing (module 3.2.P.5.2) except for the determination of purity up to and including 24 months' testing of the batches 31901 and 32444 and up to and including 3 months' testing of batch 38359:

- the calculation of *unidentified impurities* was faintly different: any unidentified impurity was calculated as per cent from the area of any unidentified peak related to the area of the trospium chloride peak in the chromatogram of the test solution; later on, a 2:1000 dilution of the test solution (0.2%) has been employed as reference solution (module 3.2.P.5.2);
- the reference solution for the determination of *benzilic acid* was a 1% solution of benzilic acid RS; later on, a 0.3% solution of benzilic acid RS has been employed (module 3.2.P.5.2).

Reporting of impurities

The results for benzilic acid and any unidentified impurity have been reported according to the Note for Guidance on Impurities in New Drug Products (CPMP/ICH/2738/99).

45 mg maximum daily dose of trospium chloride

- Reporting threshold: 0.1%
- Identification threshold: 0.2%
- Qualification threshold: 200 µg

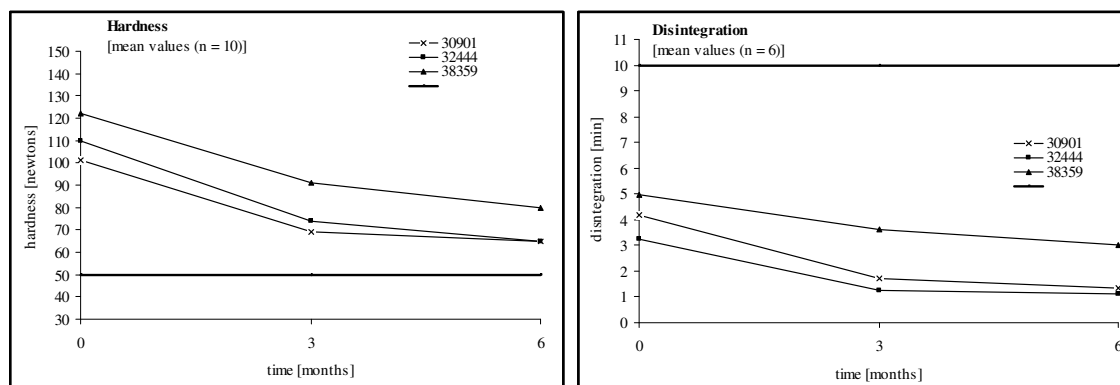
All impurities at a level greater than the reporting threshold are summed and reported as total impurities.

Results of stability studies at accelerated conditions

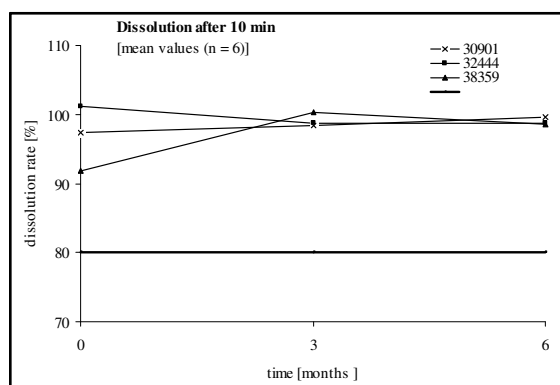
No "significant change" occurred during 6 months' testing.

The variability of data was little except for the resistance to crushing which decreased due to moisture absorbance expressed by a certain increase of tablet height and mass.

Tablet softening again was accompanied by an accelerated tablet disintegration.



There was no serious effect on the dissolution of trospium chloride.



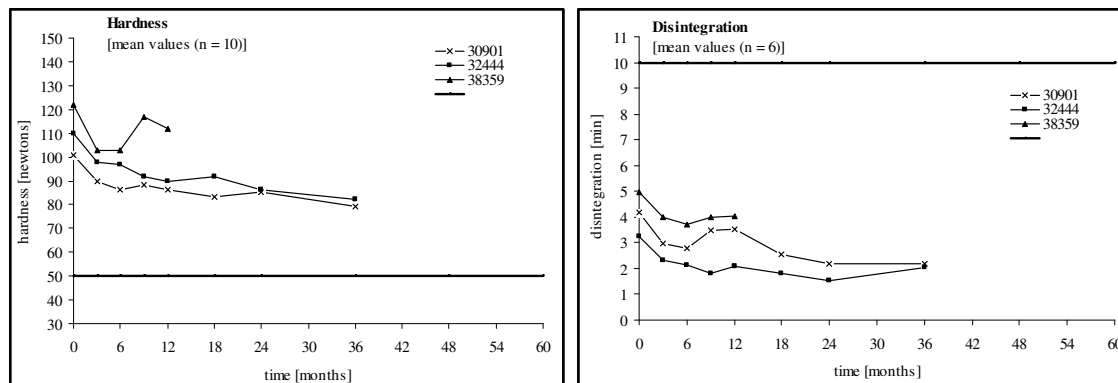
The content of benzoic acid or any other impurity was below 0.1% up to 6 months' testing except one isolated result of 0.2% estimated after 6 months for batch 31901. This "impurity" in question was identified by a relative retention of about 2.3 but must, in retrospective, be explained as analytical error for the same reasons cited for the OOS result estimated for batch 32444 after 6 months at long-term testing.

The results for the assay of trospium chloride ranged around 100% of the label content.

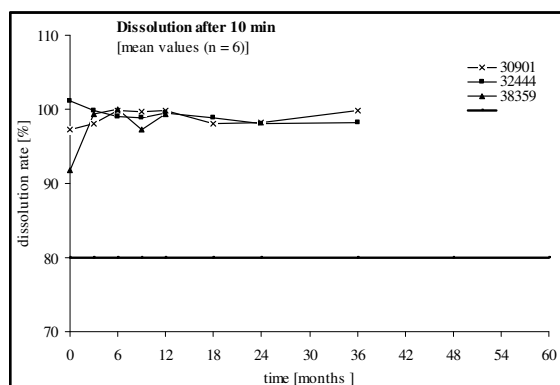
Subdivision of tablets and microbiological quality complied with the tests at start and end of shelf-life testing.

Results of stability studies at intermediate conditions

No "significant change" occurred during 36 months' testing and the variability of data was little. The changes of tablet hardness and disintegration were less conspicuous.



There was no serious effect on the dissolution of trospium chloride.



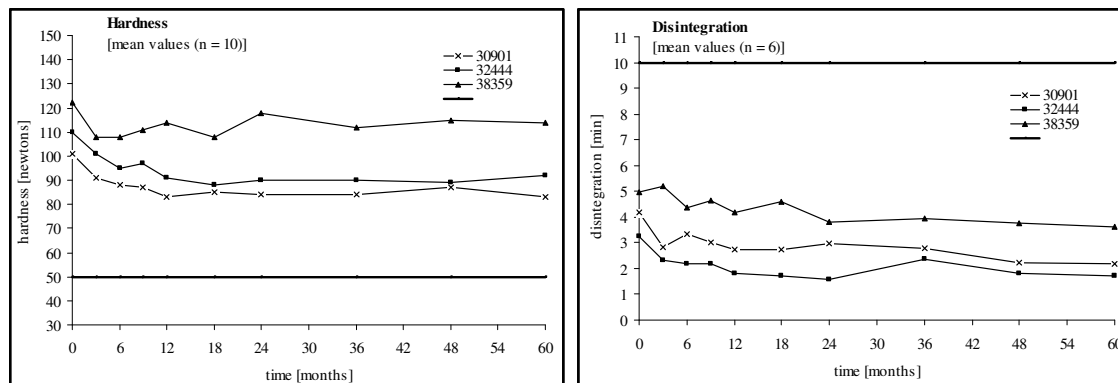
The content of benzoic acid or any other impurity was below 0.1% up to 36 months' testing.

The results for the assay of trospium chloride ranged around 100% of the label content.

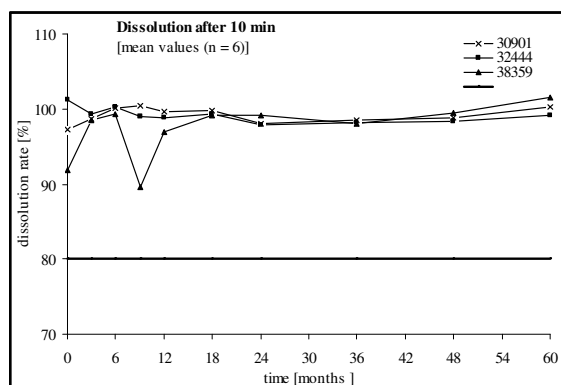
Subdivision of tablets and microbiological quality complied with the tests at start and end of shelf-life testing.

Results of stability studies at long-term conditions (25°C, 60% RH)

No "significant change" occurred during 60 months' testing and the variability of data was little. The changes of tablet hardness and disintegration were less conspicuous.



There was no serious effect on the dissolution of trospium chloride.



The content of benzoic acid and any other impurity was below 0.1% up to 60 months' testing except one isolated result of 0.3% estimated after 6 months for batch 32444. This "impurity" in question was identified by a relative retention of about 2.3 but must, in retrospective, be explained as an analytical error for not recurring later on.

It should be pointed out that this "impurity" in question was detected at a single sampling time point, namely in February 2002 at 6 months' testing of batch 31901 (sample stored at accelerated conditions) and batch 32444 (sample stored at long-term conditions). Hence the results must be explained as an analytical error.

The results for the assay of trospium chloride ranged around 100% of the label content.

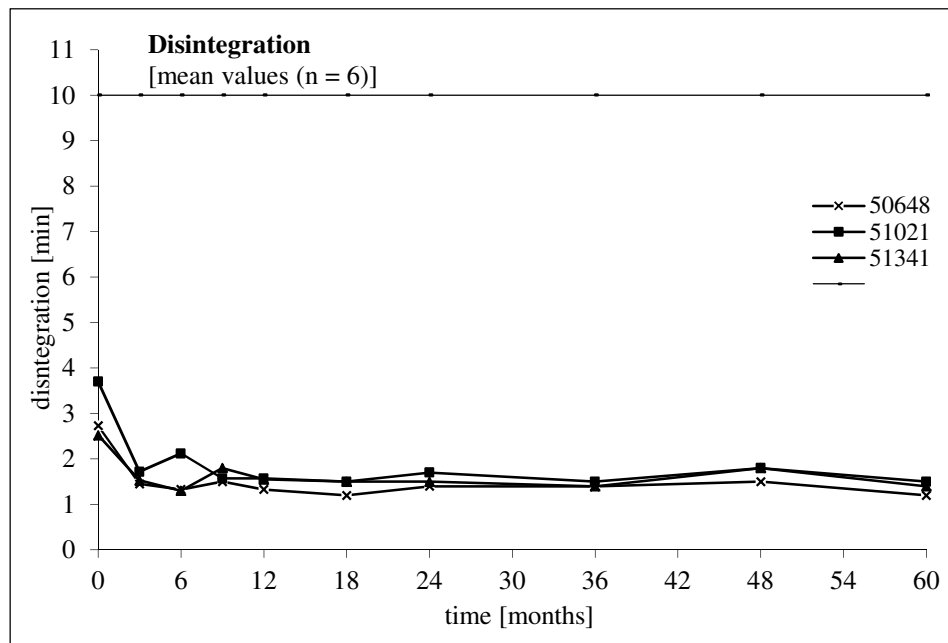
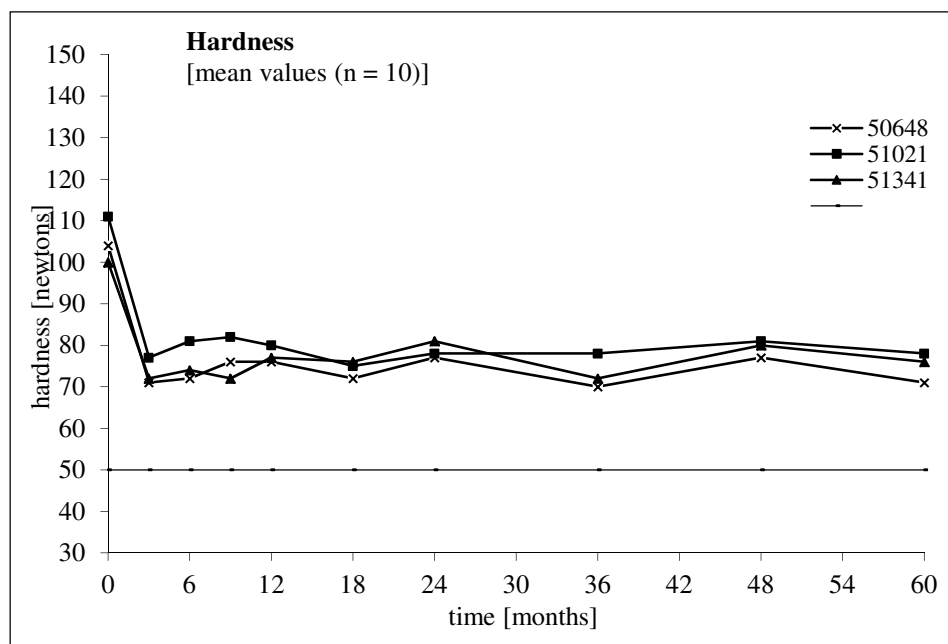
Subdivision of tablets and microbiological quality complied with the tests at start and end of shelf-life testing.

Results of stability studies at long-term conditions (30°C, 75% RH)

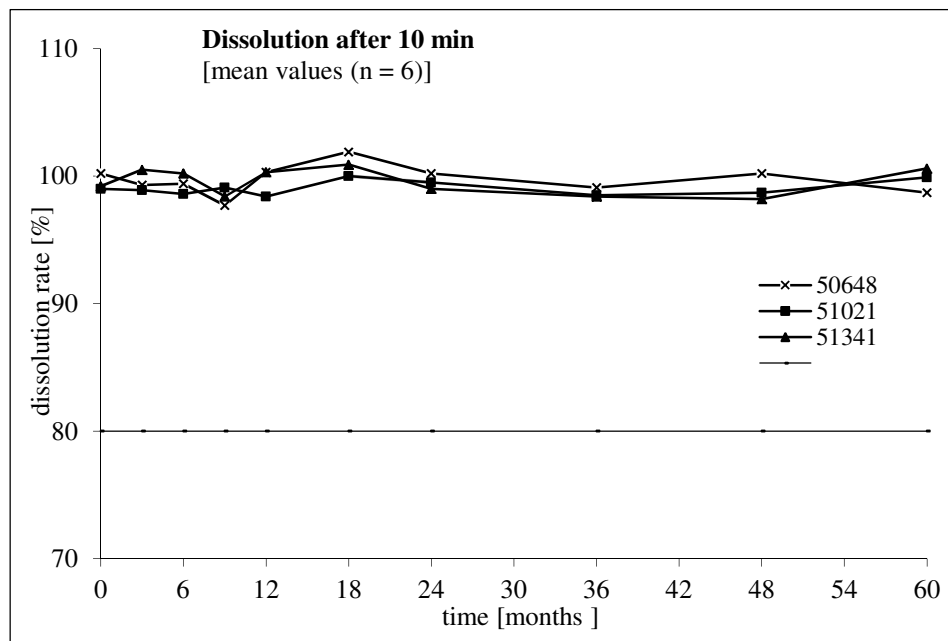
No "significant change" occurred during 60 months' testing.

The variability of data was little except for the resistance to crushing which decreased due to moisture absorbance expressed by a certain increase of tablet height and mass.

Tablet softening again was accompanied by an accelerated tablet disintegration.



There was no serious effect on the dissolution of trospium chloride.



The content of benzoic acid or any other impurity was below 0.1%.

The results for the assay of trospium chloride ranged around 100% of the label content.

Subdivision of tablets and microbiological quality complied with the tests at start of shelf-life testing.

Conclusions

The shelf-life of drug product is 5 years.

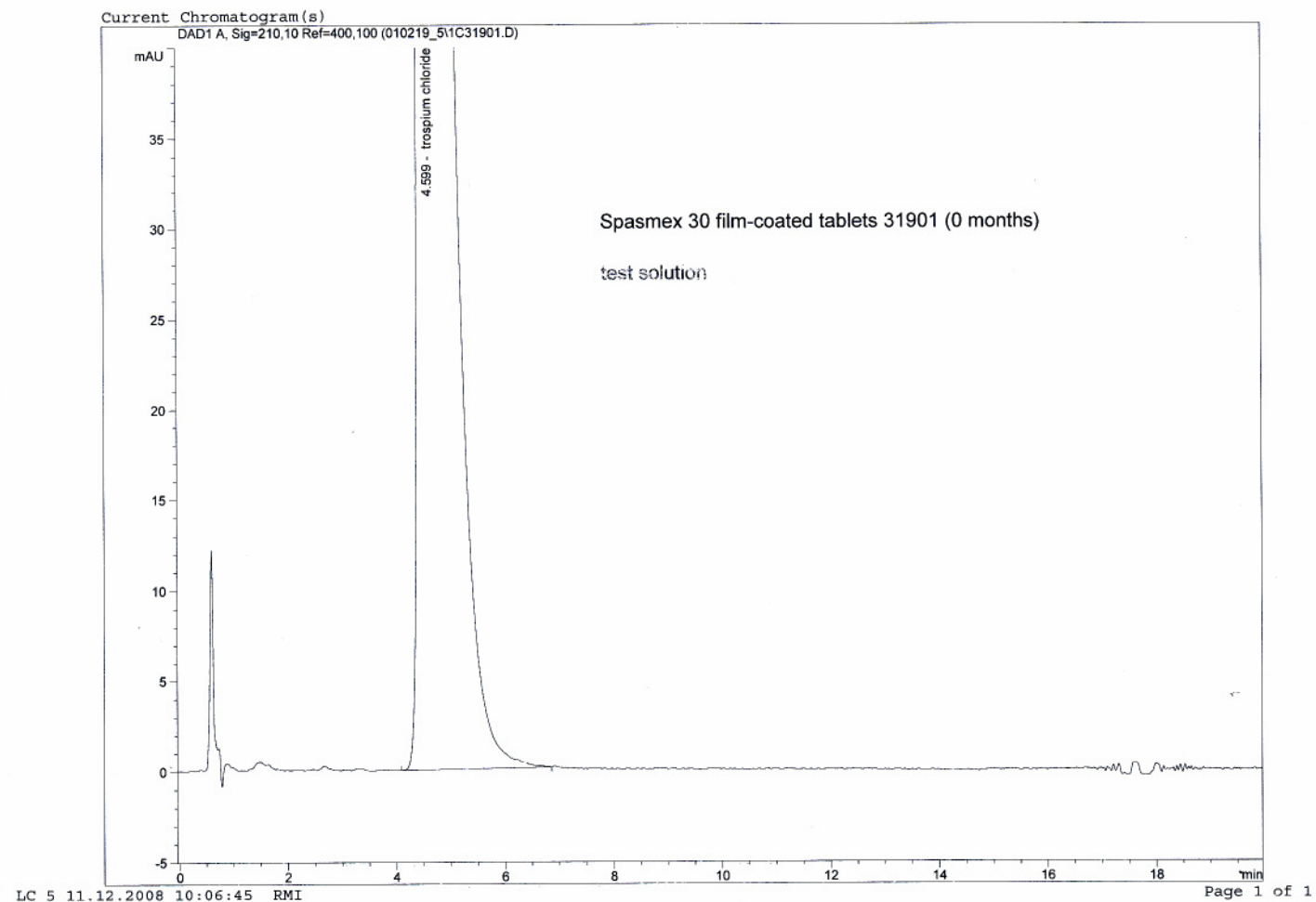
A labelling statement is recommended ("Store below 30°C.").

Trospium chloride 30 mg
Film-coated tablets

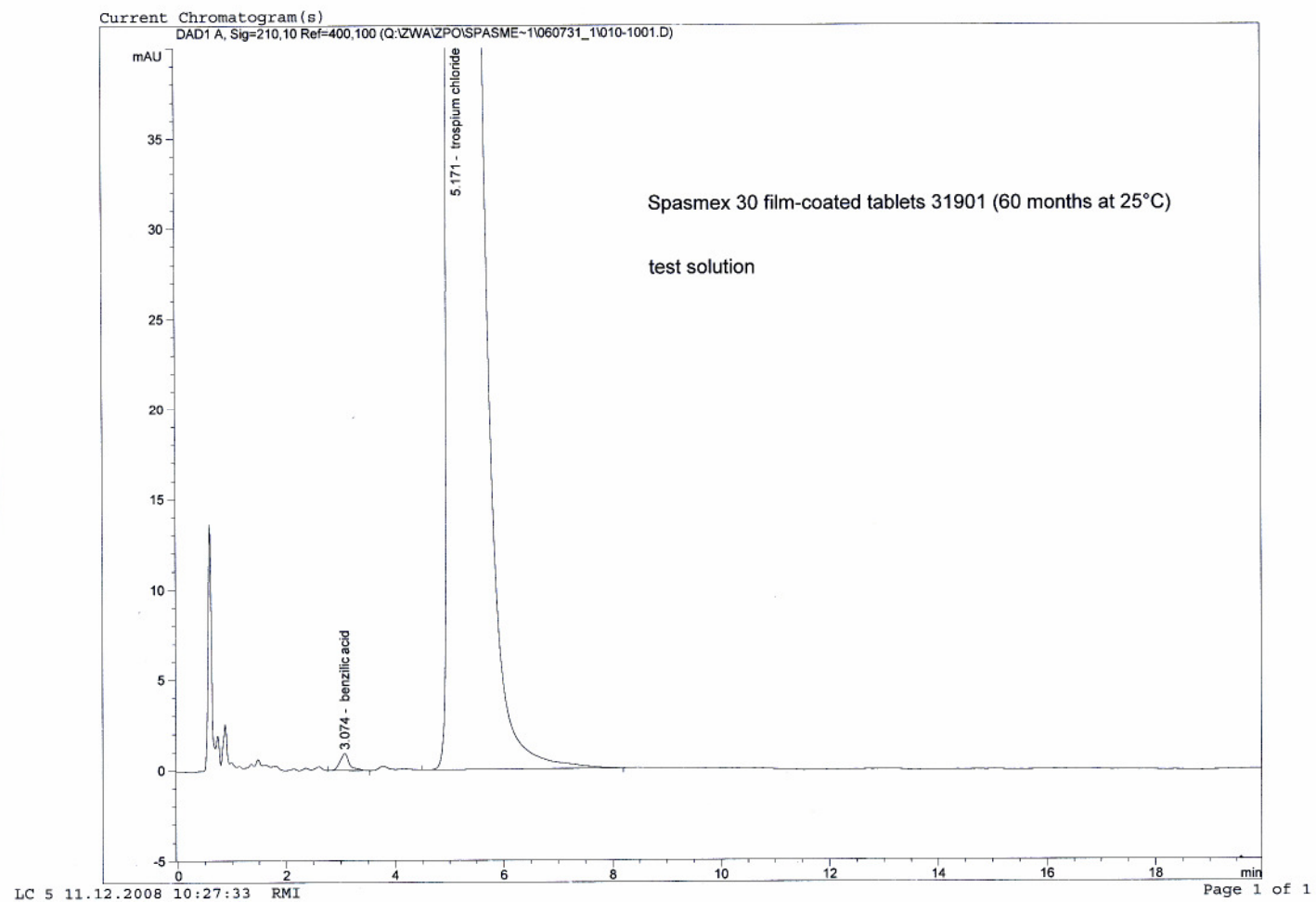
Module
3.2.P.8.3
Stability Data

Drug product	Trospium chloride 30 mg	Storage conditions		25°C ± 2°C, 60% ± 5 % RH							
Dosage form	Film-coated tablets	Container closure system		Alu/PVC blister							
Manufacturer	Dr. R. Pflieger Chemische Fabrik GmbH	Date of storage		08.2001							
Batch number	31901										
Batch size	275 kg										
Date of manufacture	13.02.2001										
		MONTHS									
Test	Specification	0	3	6	9	12	18	24	36	48	60
Description	almost white, odourless film-coated tablets, round and biconvex, snap-tab score on one side, 9 mm in diameter	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Height	3.4 – 4.1 mm	3.8 mm	3.9 mm	3.8 mm	3.8 mm	3.8 mm	3.8 mm	3.8 mm	3.8 mm	3.8 mm	3.8 mm
Uniformity of mass	complies (Ph.Eur. 2.9.5)	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Average mass	246.6 – 272.6 mg	257.0 mg	260.7 mg	261.3 mg	262.4 mg	260.2 mg	263.4 mg	262.4 mg	261.7 mg	261.3 mg	261.2 mg
Resistance to crushing	≥ 50 N	101 N	91 N	88 N	87 N	83 N	85 N	84 N	84 N	87 N	83 N
Disintegration	≤ 10 min	4' 10"	2' 51"	3' 19"	3' 00"	2' 44"	2' 43"	2' 57"	2' 46"	2' 13"	2' 12"
Subdivision	complies (Ph.Eur. 2.9.5)	-	-	-	-	-	complies	-	complies	complies	complies
Dissolution											
Trospium chloride	≥ 80% after 10 min	97.3%	98.7%	100.1%	100.4%	99.6%	99.8%	98.1%	98.6%	98.9%	100.3%
Identification											
Trospium chloride	positive (HPLC)	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Purity											
Benzilic acid	≤ 0.3%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%
Any unidentified	≤ 0.2%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%
Unidentified total	≤ 0.5%	0	0	0	0	0	0	0	0	0	0
Total impurities	≤ 0.8%	0	0	0	0	0	0	0	0	0	0
Assay											
Trospium chloride	95.0% – 105.0%	98.2%	100.3%	99.4%	99.3%	98.1%	99.1%	99.9%	99.4%	99.7%	98.9%
Microbiological quality	complies (Ph.Eur. 5.1.4, 3A)	complies	-	-	-	-	-	-	complies	-	complies

Print of window 38: Current Chromatogram(s)



Print of window 38: Current Chromatogram(s)



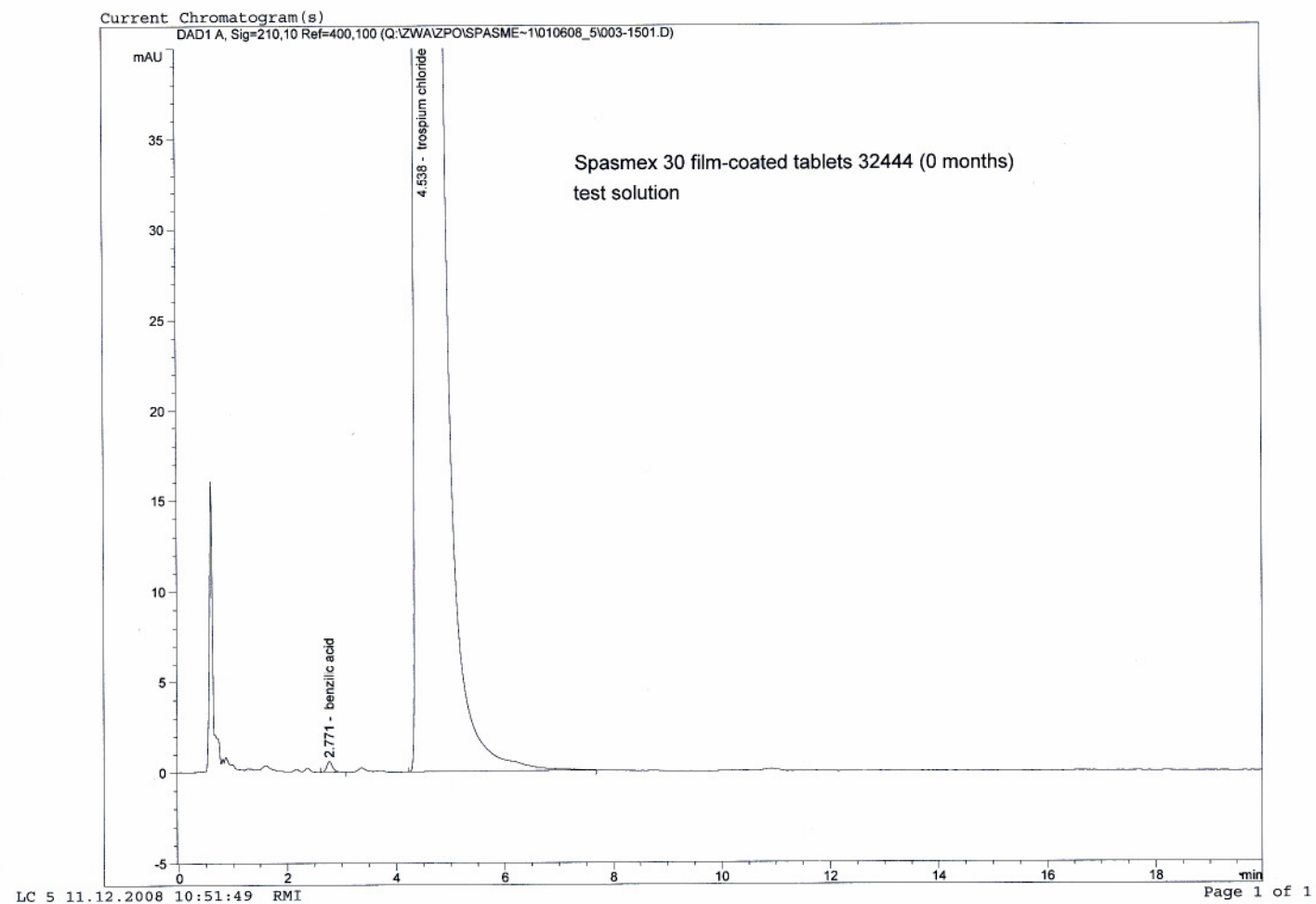
Trospium chloride 30 mg
Film-coated tablets

Module
3.2.P.8.3
Stability Data

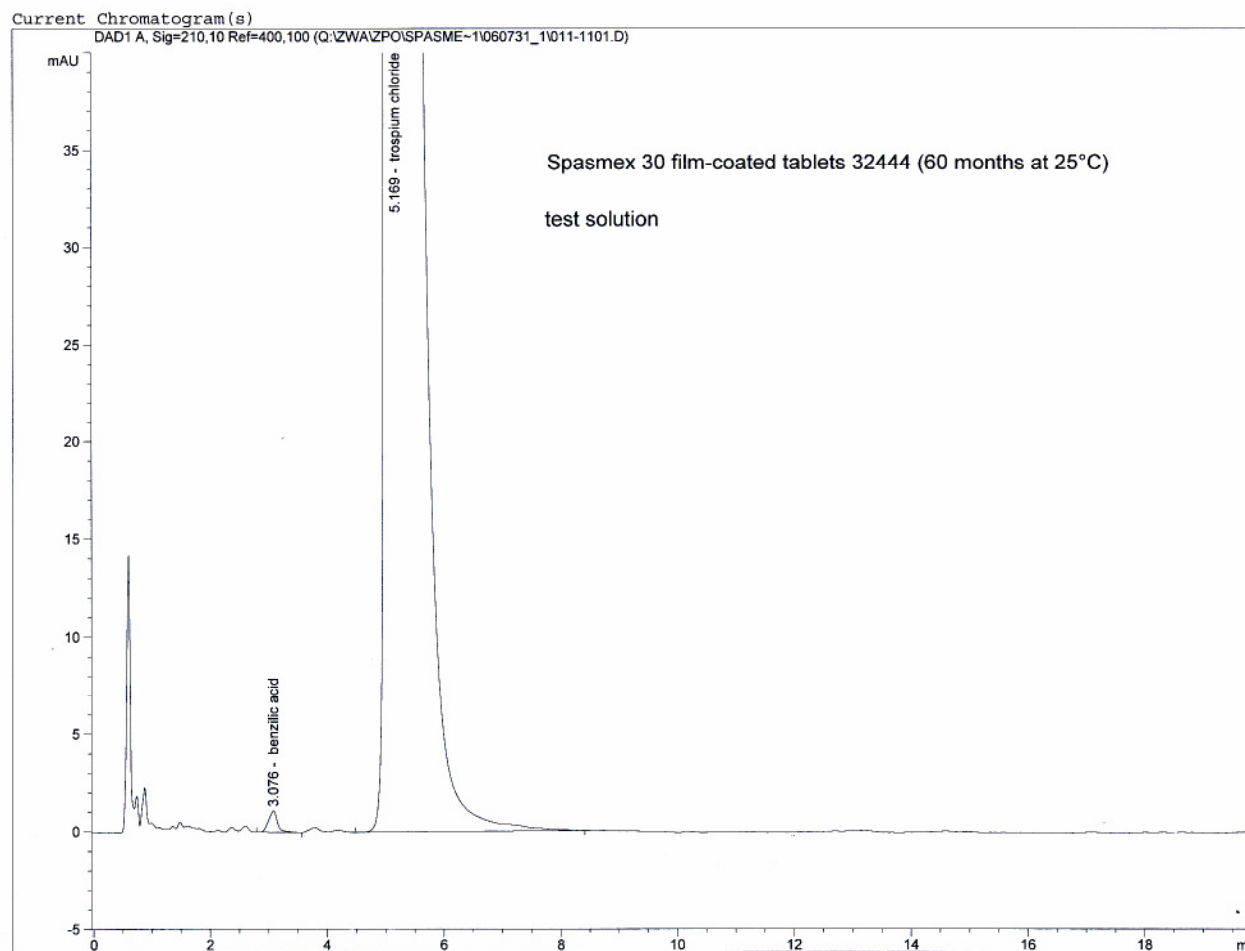
Drug product	Trospium chloride 30 mg	Storage conditions		25°C ± 2°C, 60% ± 5 % RH							
Dosage form	Film-coated tablets	Container closure system		Alu/PVC blister							
Manufacturer	Dr. R. Pflieger Chemische Fabrik GmbH	Date of storage		08.2001							
Batch number	32444										
Batch size	550 kg										
Date of manufacture	22.05.2001										
		MONTHS									
Test	Specification	0	3	6	9	12	18	24	36	48	60
Description	almost white, odourless film-coated tablets, round and biconvex, snap-tab score on one side, 9 mm in diameter	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Height	3.4 – 4.1 mm	3.8 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm
Uniformity of mass	complies (Ph.Eur. 2.9.5)	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Average mass	246.6 – 272.6 mg	259.5 mg	260.7 mg	262.1 mg	262.7 mg	262.5 mg	262.3 mg	263.0 mg	262.3 mg	262.4 mg	262.1 mg
Resistance to crushing	≥ 50 N	110 N	101 N	95 N	97 N	91 N	88 N	90 N	90 N	89 N	92 N
Disintegration	≤ 10 min	3'15''	2'19''	2'10''	2'11''	1'48''	1'43''	1'35''	2'21''	1'50''	1'42''
Subdivision	complies (Ph.Eur. 2.9.5)	-	-	-	-	-	complies	-	complies	complies	complies
Dissolution											
Trospium chloride	≥ 80% after 10 min	101.2%	99.3%	100.3%	99.0%	98.9%	99.4%	97.9%	98.2%	98.4%	99.1%
Identification											
Trospium chloride	positive (HPLC)	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Purity											
Benzilic acid	≤ 0.3%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%
Any unidentified	≤ 0.2%	≤ 0.1%	≤ 0.1%	0.3%*	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%
Unidentified total	≤ 0.5%	0	0	0.3%	0	0	0	0	0	0	0
Total impurities	≤ 0.8%	0	0	0.3%	0	0	0	0	0	0	0
Assay											
Trospium chloride	95.0% – 105.0%	98.8%	99.2%	99.3%	101.3%	98.7%	100.9%	99.4%	99.5%	99.0%	99.8%
Microbiological quality	complies (Ph.Eur. 5.1.4, 3A)	complies	-	-	-	-	-	-	complies	-	complies

* retention 2.3 relative to trospium chloride (in retrospective, the result must be explained as analytical error)

Print of window 38: Current Chromatogram(s)



Print of window 38: Current Chromatogram(s)

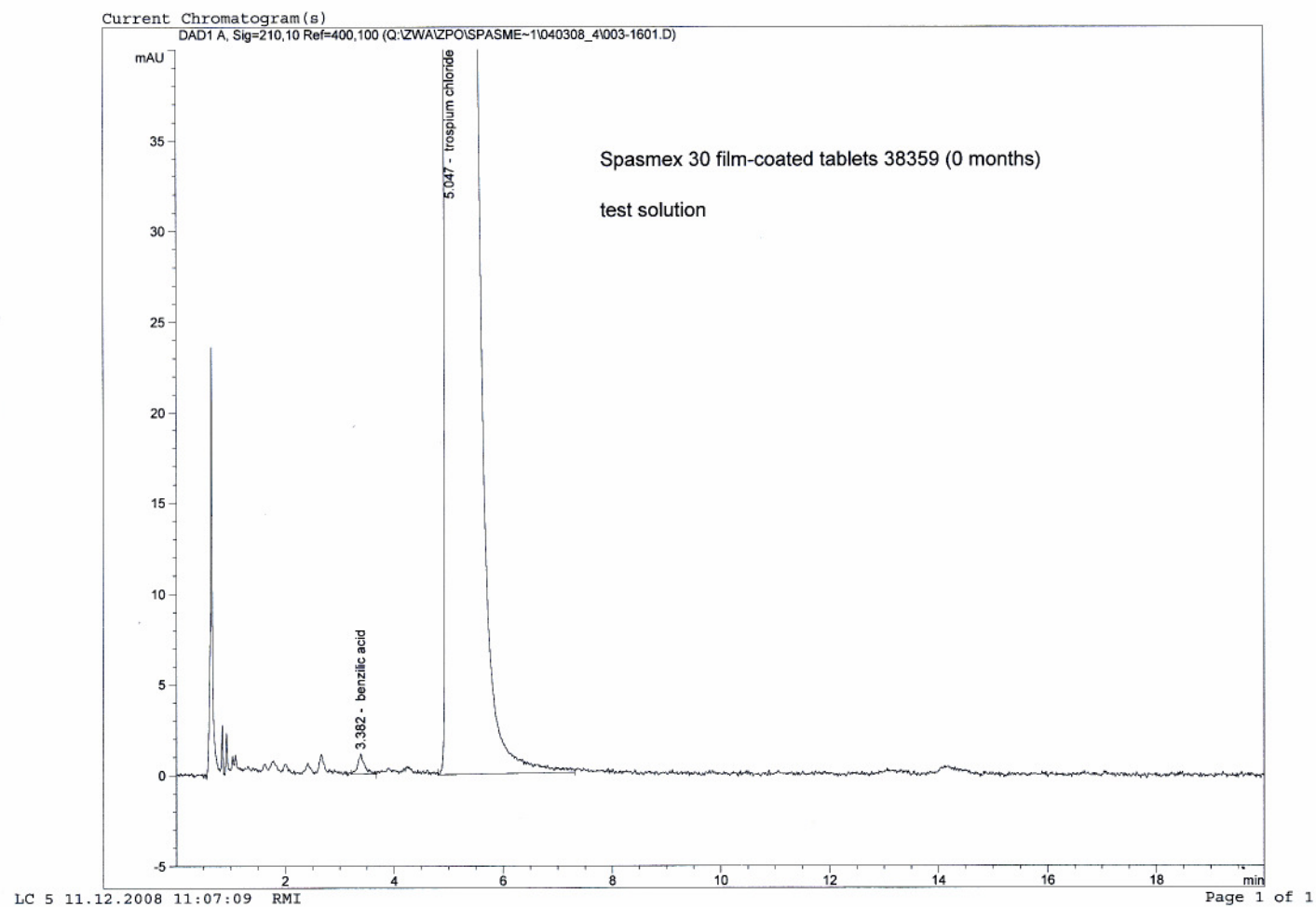


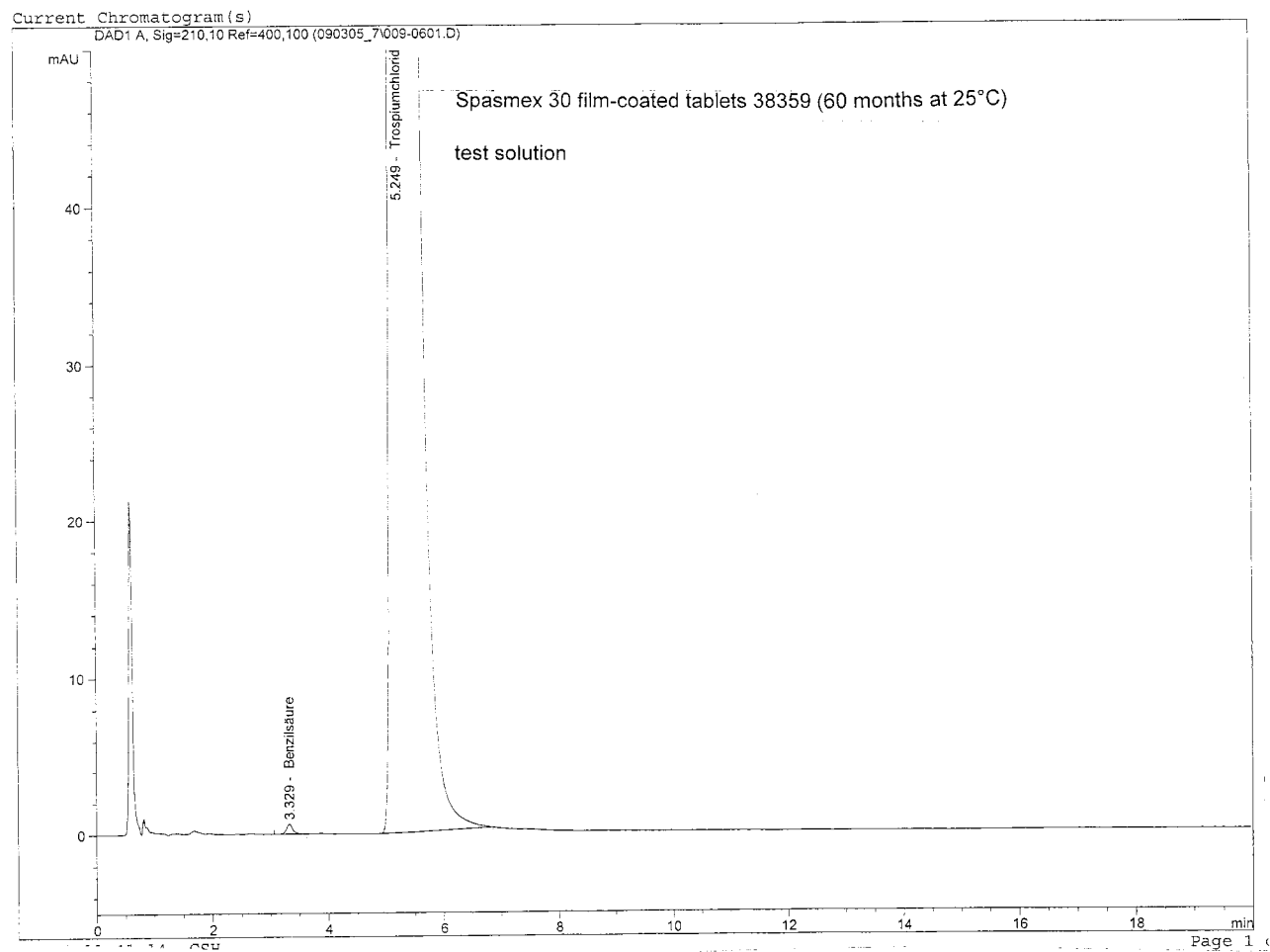
Trospium chloride 30 mg
Film-coated tablets

Module
3.2.P.8.3
Stability Data

Drug product	Trospium chloride 30 mg	Storage conditions			25°C ± 2°C, 60% ± 5% RH						
Dosage form	Film-coated tablets	Container closure system			Alu/PVC blister						
Manufacturer	Dr. R. Pflieger Chemische Fabrik GmbH	Date of storage			03.2004						
Batch number	38359										
Batch size	550 kg										
Date of manufacture	03.02.2004										
		MONTHS									
Test	Specification	0	3	6	9	12	18	24	36	48	60
Description	almost white, odourless film-coated tablets, round and biconvex, snap-tab score on one side, 9 mm in diameter	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Height	3.4 – 4.1 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	4.0 mm	3.9 mm	4.0 mm	4.0 mm	4.0 mm	4.0 mm
Uniformity of mass	complies (Ph.Eur. 2.9.5)	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Average mass	246.6 – 272.6 mg	261.0 mg	262.7 mg	262.1 mg	262.8 mg	263.4 mg	262.9 mg	262.6 mg	263.3 mg	261.4 mg	262.8 mg
Resistance to crushing	≥ 50 N	122 N	108 N	108 N	111 N	114 N	108 N	118 N	112 N	115 N	113 N
Disintegration	≤ 10 min	4' 57"	5' 12"	4' 23"	4' 39"	4' 10"	4' 35"	3' 48"	3' 57"	3' 45"	3' 36"
Subdivision	complies (Ph.Eur. 2.9.5)	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Dissolution											
Trospium chloride	≥ 80% after 10 min	91.8%	98.5%	99.4%	89.6%	97.0%	99.1%	99.1%	98.1%	99.5%	101.5%
Identification											
Trospium chloride	positive (HPLC)	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Purity											
Benzilic acid	≤ 0.3%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%
Any unidentified	≤ 0.2%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%
Unidentified total	≤ 0.5%	0	0	0	0	0	0	0	0	0	0
Total impurities	≤ 0.8%	0	0	0	0	0	0	0	0	0	0
Assay											
Trospium chloride	95.0% – 105.0%	98.0%	99.0%	96.7%	99.3%	100.8%	98.2%	99.8%	100.9%	100.4%	100.3%
Microbiological quality	complies (Ph.Eur. 5.1.4, 3A)	complies	-	-	-	-	-	-	complies	-	complies

Print of window 38: Current Chromatogram(s)



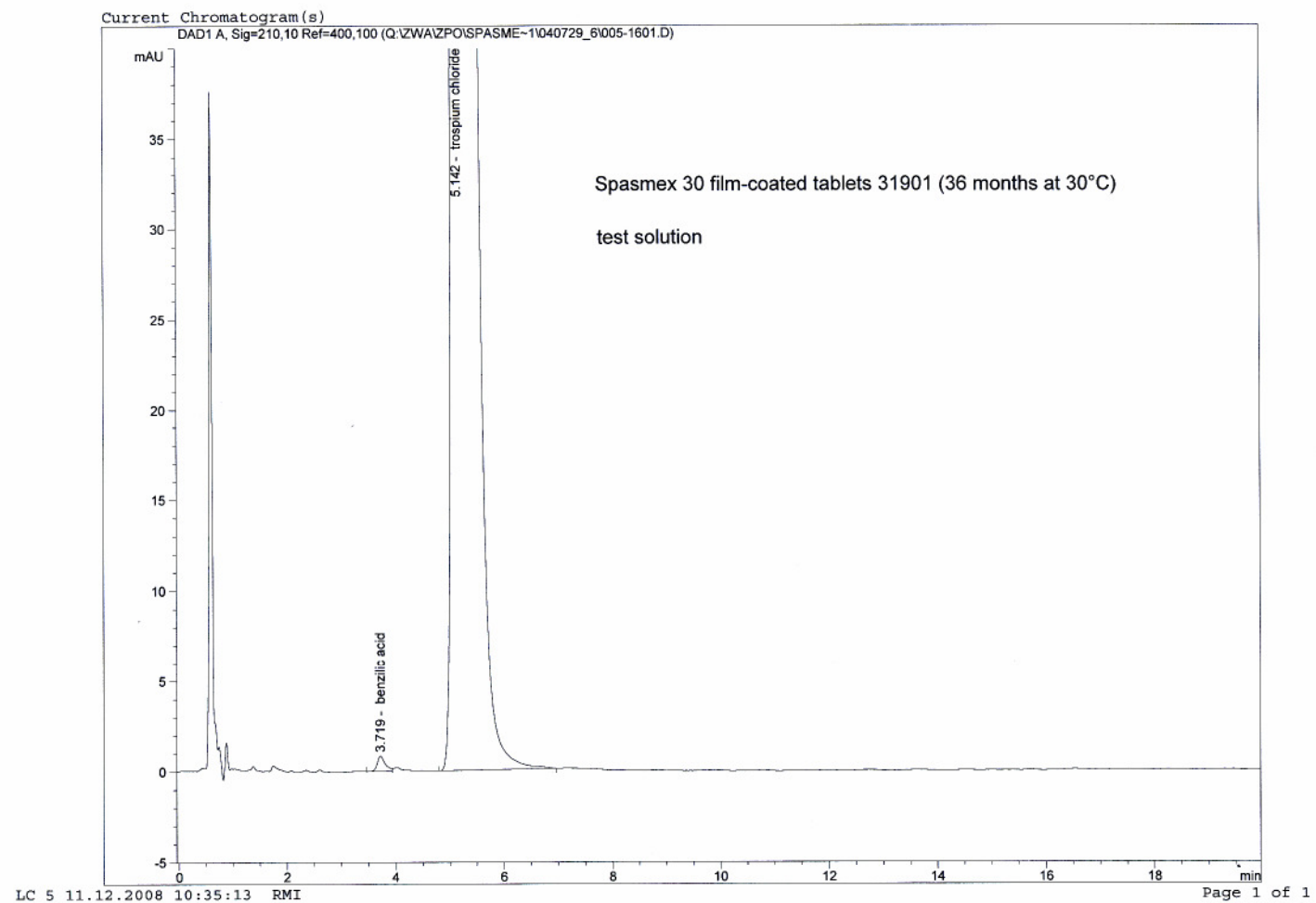


Trospium chloride 30 mg
Film-coated tablets

Module
3.2.P.8.3
Stability Data

Drug product	Trospium chloride 30 mg	Storage conditions		30°C ± 2°C, 65% ± 5% RH							
Dosage form	Film-coated tablets	Container closure system		Alu/PVC blister							
Manufacturer	Dr. R. Pflieger Chemische Fabrik GmbH	Date of storage		08.2001							
Batch number	31901										
Batch size	275 kg										
Date of manufacture	13.02.2001										
		MONTHS									
Test	Specification	0	3	6	9	12	18	24	36	48	60
Description	almost white, odourless film-coated tablets, round and biconvex, snap-tab score on one side, 9 mm in diameter	complies	complies	complies	complies	complies	complies	complies	complies	-	-
Height	3.4 – 4.1 mm	3.8 mm	3.9 mm	3.9 mm	3.8 mm	3.8 mm	3.8 mm	3.9 mm	3.9 mm	-	-
Uniformity of mass	complies (Ph.Eur. 2.9.5)	complies	complies	complies	complies	complies	complies	complies	complies	-	-
Average mass	246.6 – 272.6 mg	257.0 mg	260.1 mg	261.5 mg	262.0 mg	261.9 mg	262.7 mg	262.9 mg	262.3 mg	-	-
Resistance to crushing	≥ 50 N	101 N	90 N	86 N	88 N	86 N	83 N	85 N	79 N	-	-
Disintegration	≤ 10 min	4'10''	2'57''	2'46''	2'30''	2'32''	2'33''	2'10''	2'33''	-	-
Subdivision	complies (Ph.Eur. 2.9.5)	-	-	-	-	-	complies	-	complies	-	-
Dissolution											
Trospium chloride	≥ 80% after 10 min	97.3%	98.0%	99.9%	99.7%	99.8%	98.1%	98.3%	99.9%	-	-
Identification											
Trospium chloride	positive (HPLC)	complies	complies	complies	complies	complies	complies	complies	complies	-	-
Purity											
Benzilic acid	≤ 0.3%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	-	-
Any unidentified	≤ 0.2%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	-	-
Unidentified total	≤ 0.5%	0	0	0	0	0	0	0	0	-	-
Total impurities	≤ 0.8%	0	0	0	0	0	0	0	0	-	-
Assay											
Trospium chloride	95.0% – 105.0%	98.2%	99.7%	99.6%	100.4%	99.1%	98.1%	99.9%	99.7%	-	-
Microbiological quality	complies (Ph.Eur. 5.1.4, 3A)	complies	-	-	-	complies	-	-	complies	-	-

Print of window 38: Current Chromatogram(s)

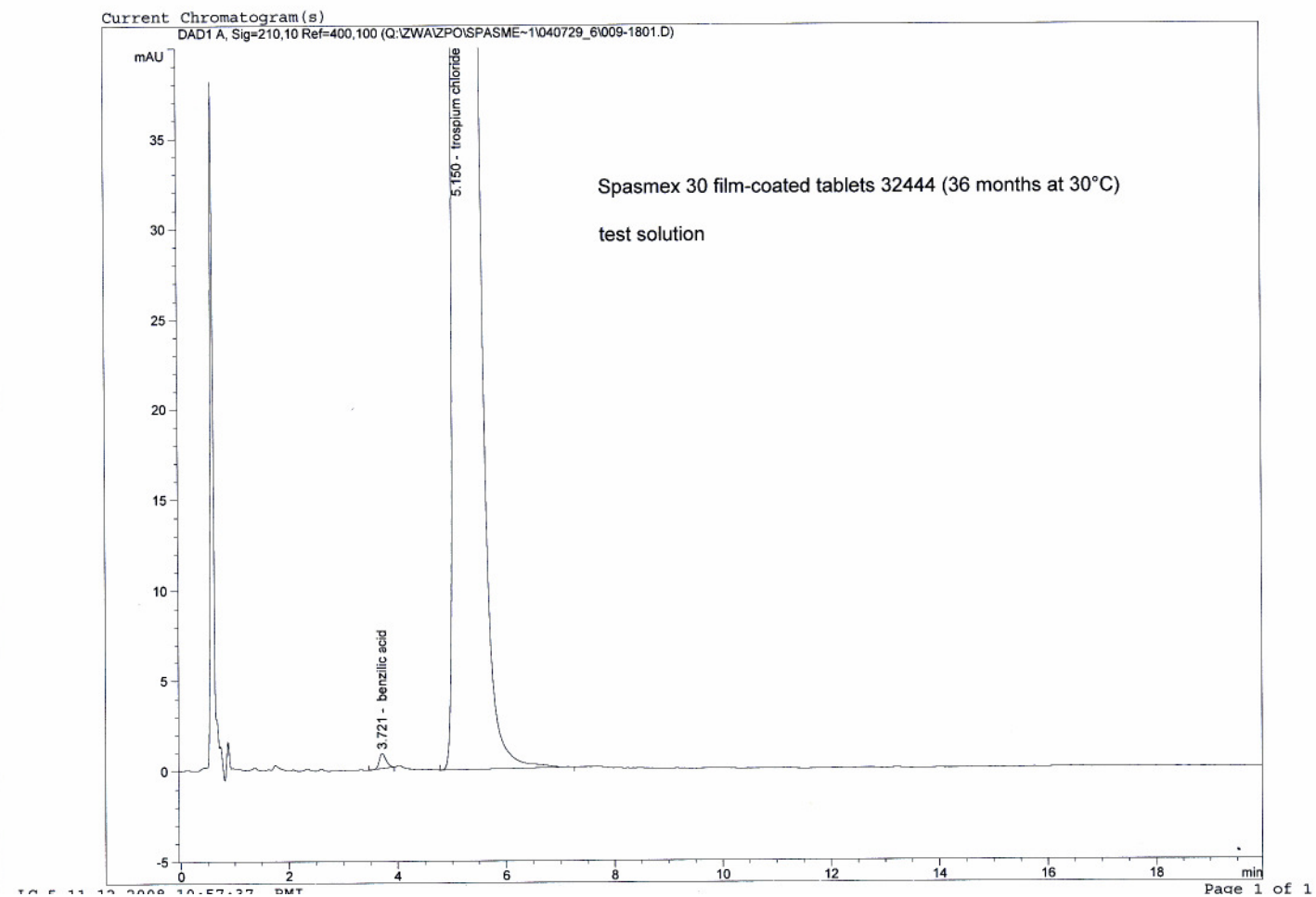


Trospium chloride 30 mg
Film-coated tablets

Module
3.2.P.8.3
Stability Data

Drug product	Trospium chloride 30 mg	Storage conditions		30°C ± 2°C, 65% ± 5% RH							
Dosage form	Film-coated tablets	Container closure system		Alu/PVC blister							
Manufacturer	Dr. R. Pflieger Chemische Fabrik GmbH	Date of storage		08.2001							
Batch number	32444										
Batch size	550 kg										
Date of manufacture	22.05.2001										
		MONTHS									
Test	Specification	0	3	6	9	12	18	24	36	48	60
Description	almost white, odourless film-coated tablets, round and biconvex, snap-tab score on one side, 9 mm in diameter	complies	complies	complies	complies	complies	complies	complies	complies	-	-
Height	3.4 – 4.1 mm	3.8 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	-	-
Uniformity of mass	complies (Ph.Eur. 2.9.5)	complies	complies	complies	complies	complies	complies	complies	complies	-	-
Average mass	246.6 – 272.6 mg	259.5 mg	261.4 mg	262.4 mg	262.5 mg	263.3 mg	262.4 mg	263.0 mg	264.0 mg	-	-
Resistance to crushing	≥ 50 N	110 N	98 N	97 N	92 N	90 N	92 N	86 N	82 N	-	-
Disintegration	≤ 10 min	3'15''	2'20''	2'08''	1'49''	2'05''	1'48''	1'33''	2'01''	-	-
Subdivision	complies (Ph.Eur. 2.9.5)	-	-	-	-	-	complies	-	complies	-	-
Dissolution											
Trospium chloride	≥ 80% after 10 min	101.2%	99.8%	99.0%	98.8%	99.5%	98.8%	98.0%	98.%2	-	-
Identification											
Trospium chloride	positive (HPLC)	complies	complies	complies	complies	complies	complies	complies	complies	-	-
Purity											
Benzilic acid	≤ 0.3%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	-	-
Any unidentified	≤ 0.2%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	-	-
Unidentified total	≤ 0.5%	0	0	0	0	0	0	0	0	-	-
Total impurities	≤ 0.8%	0	0	0	0	0	0	0	0	-	-
Assay											
Trospium chloride	95.0% – 105.0%	98.8%	99.7%	101.8%	100.6%	99.8%	98.9%	100.1%	99.7%	-	-
Microbiological quality	complies (Ph.Eur. 5.1.4, 3A)	complies	-	-	-	complies	-	-	complies	-	-

Print of window 38: Current Chromatogram(s)

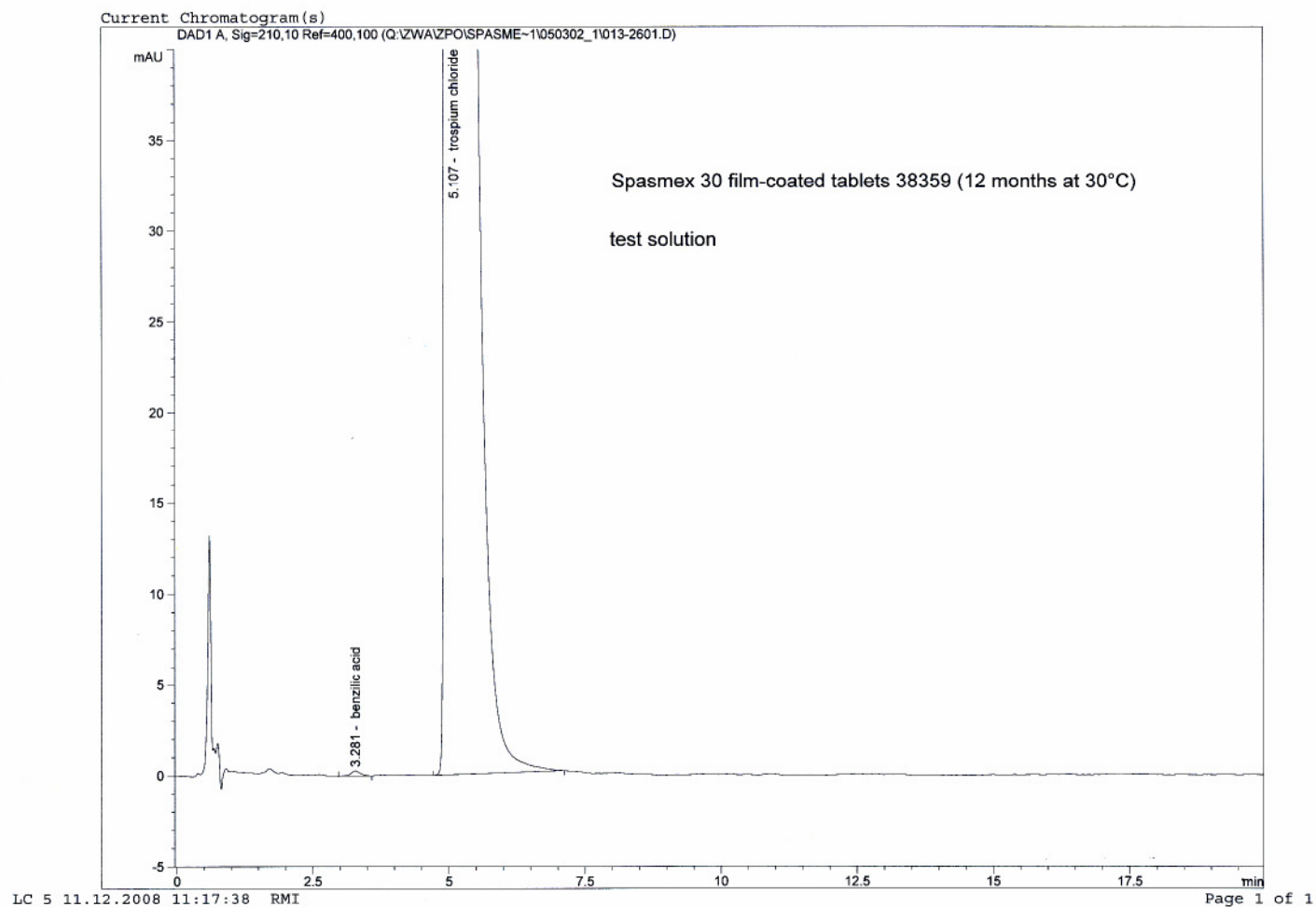


Trospium chloride 30 mg
Film-coated tablets

Module
3.2.P.8.3
Stability Data

Drug product	Trospium chloride 30 mg	Storage conditions		30°C ± 2°C, 65% ± 5% RH							
Dosage form	Film-coated tablets	Container closure system		Alu/PVC blister							
Manufacturer	Dr. R. Pflieger Chemische Fabrik GmbH	Date of storage		03.2004							
Batch number	38359										
Batch size	550 kg										
Date of manufacture	03.02.2004										
		MONTHS									
Test	Specification	0	3	6	9	12	18	24	36	48	60
Description	almost white, odourless film-coated tablets, round and biconvex, snap-tab score on one side, 9 mm in diameter	complies	complies	complies	complies	complies	-	-	-	-	-
Height	3.4 – 4.1 mm	3.9 mm	3.9 mm	3.9 mm	4.0 mm	3.9 mm	-	-	-	-	-
Uniformity of mass	complies (Ph.Eur. 2.9.5)	complies	complies	complies	complies	complies	-	-	-	-	-
Average mass	246.6 – 272.6 mg	261.0 mg	263.0 mg	262.7 mg	263.5 mg	262.9 mg	-	-	-	-	-
Resistance to crushing	≥ 50 N	122 N	103 N	103 N	117 N	112 N	-	-	-	-	-
Disintegration	≤ 10 min	4' 57"	3' 59"	3' 43"	4' 00"	4' 02"	-	-	-	-	-
Subdivision	complies (Ph.Eur. 2.9.5)	complies	complies	complies	complies	complies	-	-	-	-	-
Dissolution											
Trospium chloride	≥ 80% after 10 min	91.8%	99.4%	100.0%	97.2%	99.4%	-	-	-	-	-
Identification											
Trospium chloride	positive (HPLC)	complies	complies	complies	complies	complies	-	-	-	-	-
Purity											
Benzilic acid	≤ 0.3%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	-	-	-	-	-
Any unidentified	≤ 0.2%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	≤ 0.1%	-	-	-	-	-
Unidentified total	≤ 0.5%	0	0	0	0	0	-	-	-	-	-
Total impurities	≤ 0.8%	0	0	0	0	0	-	-	-	-	-
Assay											
Trospium chloride	95.0% – 105.0%	98.0%	100.4%	98.9%	100.7%	99.9%	-	-	-	-	-
Microbiological quality	complies (Ph.Eur. 5.1.4, 3A)	complies	-	-	-	complies	-	-	-	-	-

Print of window 38: Current Chromatogram(s)



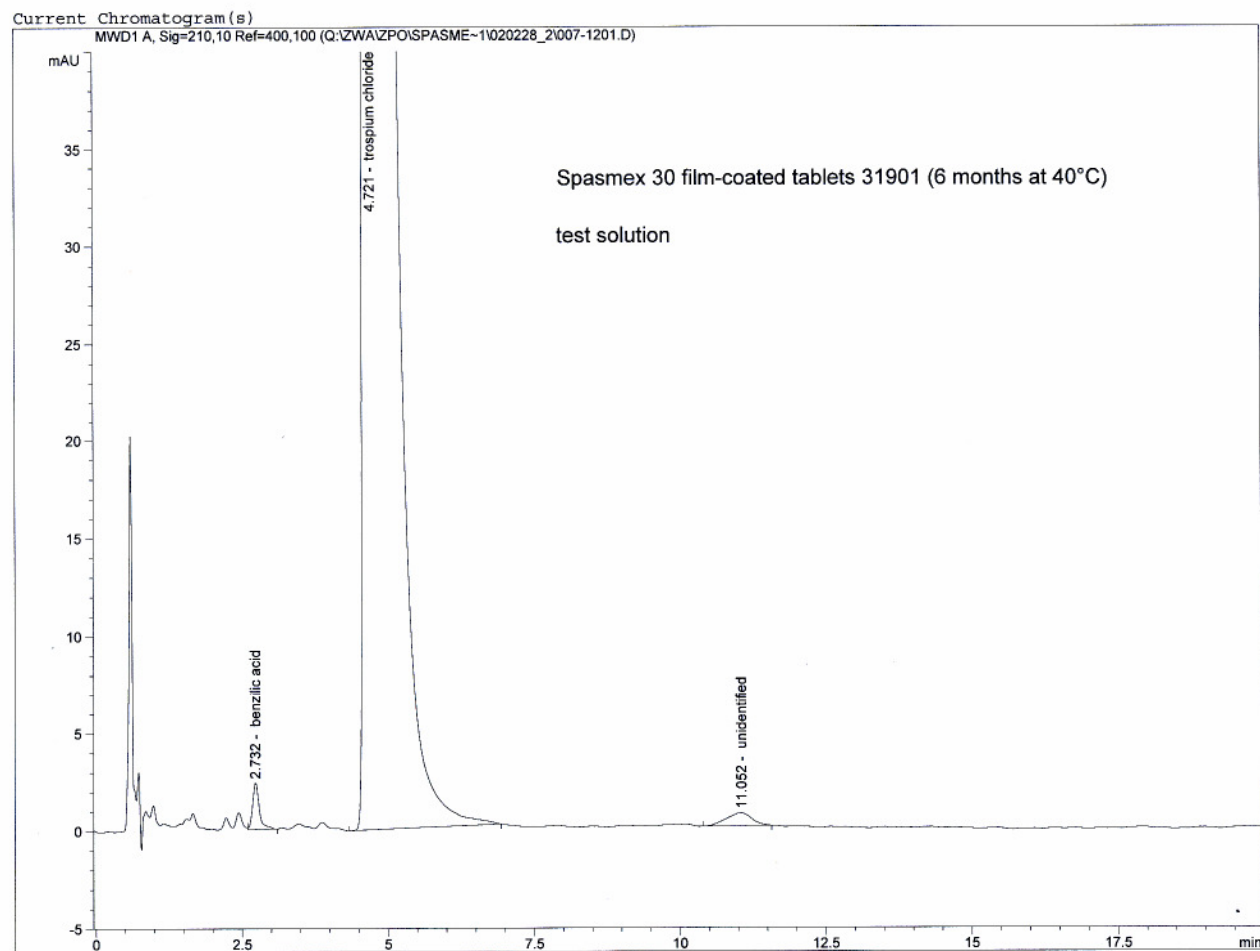
Trospium chloride 30 mg
Film-coated tablets

Module
3.2.P.8.3
Stability Data

Drug product	Trospium chloride 30 mg	Storage conditions		40°C ± 2°C, 75% ± 5 % RH							
Dosage form	Film-coated tablets	Container closure system		Alu/PVC blister							
Manufacturer	Dr. R. Pflieger Chemische Fabrik GmbH	Date of storage		08.2001							
Batch number	31901										
Batch size	275 kg										
Date of manufacture	13.02.2001										
		MONTHS									
Test	Specification	0	3	6	9	12	18	24	36	48	60
Description	almost white, odourless film-coated tablets, round and biconvex, snap-tab score on one side, 9 mm in diameter	complies	complies	complies	-	-	-	-	-	-	-
Height	3.4 – 4.1 mm	3.8 mm	4.0 mm	4.0 mm	-	-	-	-	-	-	-
Uniformity of mass	complies (Ph.Eur. 2.9.5)	complies	complies	complies	-	-	-	-	-	-	-
Average mass	246.6 – 272.6 mg	257.0 mg	263.2 mg	262.4 mg	-	-	-	-	-	-	-
Resistance to crushing	≥ 50 N	101 N	69 N	65 N	-	-	-	-	-	-	-
Disintegration	≤ 10 min	4'10''	1'42''	1'21''	-	-	-	-	-	-	-
Dissolution											
Trospium chloride	≥ 80% after 10 min	97.3%	98.4%	99.6%	-	-	-	-	-	-	-
Identification											
Trospium chloride	positive (HPLC)	complies	complies	complies	-	-	-	-	-	-	-
Purity											
Benzilic acid	≤ 0.3%	≤ 0.1%	≤ 0.1%	≤ 0.1%	-	-	-	-	-	-	-
Any unidentified	≤ 0.2%	≤ 0.1%	≤ 0.1%	0.2%*	-	-	-	-	-	-	-
Unidentified total	≤ 0.5%	0	0	0.2%	-	-	-	-	-	-	-
Total impurities	≤ 0.8%	0	0	0.2%	-	-	-	-	-	-	-
Assay											
Trospium chloride	95.0% – 105.0%	98.2%	98.6%	99.6%	-	-	-	-	-	-	-
Microbiological quality	complies (Ph.Eur. 5.1.4, 3A)	complies	-	complies	-	-	-	-	-	-	-

* retention 2.3 relative to trospium chloride (in retrospective, the result must be explained as analytical error)

Print of window 38: Current Chromatogram(s)

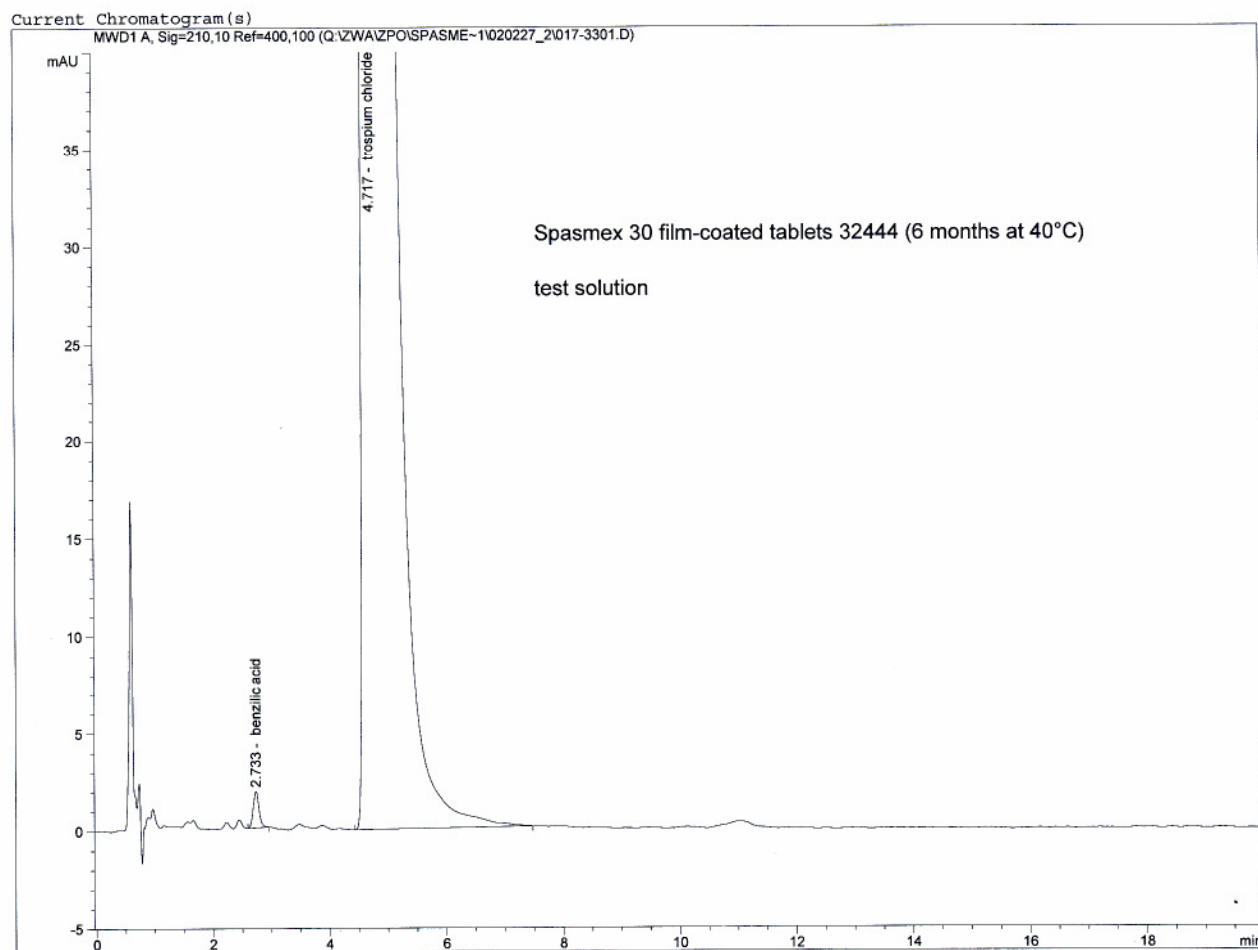


Trospium chloride 30 mg
Film-coated tablets

Module
3.2.P.8.3
Stability Data

Drug product	Trospium chloride 30 mg	Storage conditions			40°C ± 2°C, 75% ± 5 % RH						
Dosage form	Film-coated tablets	Container closure system			Alu/PVC blister						
Manufacturer	Dr. R. Pflieger Chemische Fabrik GmbH	Date of storage			08.2001						
Batch number	32444										
Batch size	550 kg										
Date of manufacture	22.05.2001										
		MONTHS									
Test	Specification	0	3	6	9	12	18	24	36	48	60
Description	almost white, odourless film-coated tablets, round and biconvex, snap-tab score on one side, 9 mm in diameter	complies	complies	complies	-	-	-	-	-	-	-
Height	3.4 – 4.1 mm	3.8 mm	4.0 mm	4.0 mm	-	-	-	-	-	-	-
Uniformity of mass	complies (Ph.Eur. 2.9.5)	complies	complies	complies	-	-	-	-	-	-	-
Average mass	246.6 – 272.6 mg	259.5 mg	263.2 mg	263.9 mg	-	-	-	-	-	-	-
Resistance to crushing	≥ 50 N	110 N	74 N	65 N	-	-	-	-	-	-	-
Disintegration	≤ 10 min	3'15''	1'15''	1'07''	-	-	-	-	-	-	-
Dissolution											
Trospium chloride	≥ 80% after 10 min	101.2%	98.7%	98.8%	-	-	-	-	-	-	-
Identification											
Trospium chloride	positive (HPLC)	complies	complies	complies	-	-	-	-	-	-	-
Purity											
Benzilic acid	≤ 0.3%	≤ 0.1%	≤ 0.1%	≤ 0.1%	-	-	-	-	-	-	-
Any unidentified	≤ 0.2%	≤ 0.1%	≤ 0.1%	≤ 0.1%	-	-	-	-	-	-	-
Unidentified total	≤ 0.5%	0	0	0	-	-	-	-	-	-	-
Total impurities	≤ 0.8%	0	0	0	-	-	-	-	-	-	-
Assay											
Trospium chloride	95.0% – 105.0%	98.8%	100.4%	101.2%	-	-	-	-	-	-	-
Microbiological quality	complies (Ph.Eur. 5.1.4, 3A)	complies	-	complies	-	-	-	-	-	-	-

Print of window 38: Current Chromatogram(s)

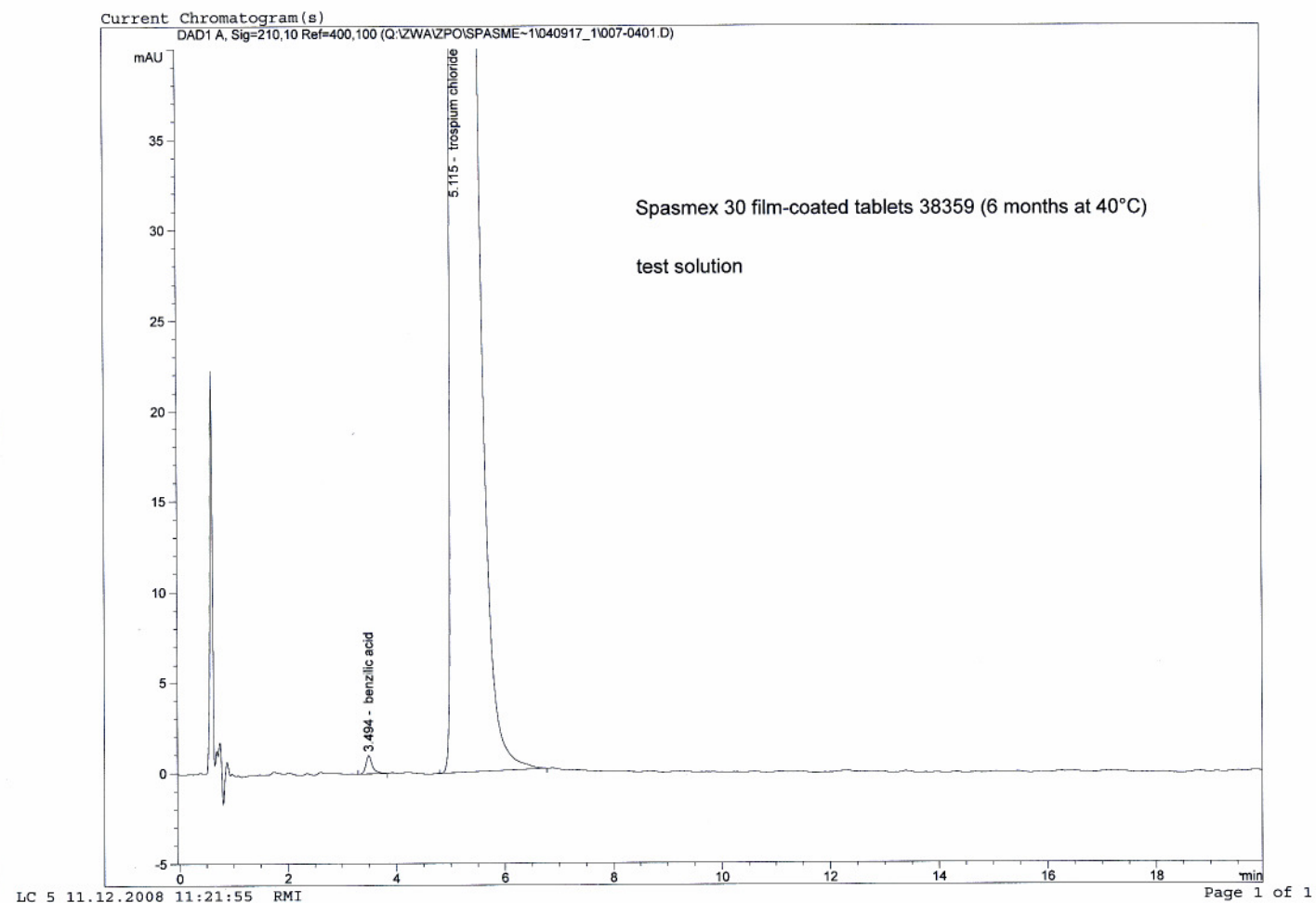


Trospium chloride 30 mg
Film-coated tablets

Module
3.2.P.8.3
Stability Data

Drug product	Trospium chloride 30 mg			Storage conditions		40°C ± 2°C, 75% ± 5% RH					
Dosage form	Film-coated tablets			Container closure system		Alu/PVC blister					
Manufacturer	Dr. R. Pflieger Chemische Fabrik GmbH			Date of storage		03.2004					
Batch number	38359										
Batch size	550 kg										
Date of manufacture	03.02.2004										
		MONTHS									
Test	Specification	0	3	6	9	12	18	24	36	48	60
Description	almost white, odourless film-coated tablets, round and biconvex, snap-tab score on one side, 9 mm in diameter	complies	complies	complies	-	-	-	-	-	-	-
Height	3.4 – 4.1 mm	3.9 mm	4.0 mm	4.0 mm	-	-	-	-	-	-	-
Uniformity of mass	complies (Ph.Eur. 2.9.5)	complies	complies	complies	-	-	-	-	-	-	-
Average mass	246.6 – 272.6 mg	261.0 mg	264.1 mg	265.2 mg	-	-	-	-	-	-	-
Resistance to crushing	≥ 50 N	122 N	91 N	80 N	-	-	-	-	-	-	-
Disintegration	≤ 10 min	4' 57"	3' 36"	3' 01"	-	-	-	-	-	-	-
Subdivision	complies (Ph.Eur. 2.9.5)	complies	complies	complies	-	-	-	-	-	-	-
Dissolution											
Trospium chloride	≥ 80% after 10 min	91.8%	100.3%	98.5%	-	-	-	-	-	-	-
Identification											
Trospium chloride	positive (HPLC)	complies	complies	complies	-	-	-	-	-	-	-
Purity											
Benzilic acid	≤ 0.3%	≤ 0.1%	≤ 0.1%	≤ 0.1%	-	-	-	-	-	-	-
Any unidentified	≤ 0.2%	≤ 0.1%	≤ 0.1%	≤ 0.1%	-	-	-	-	-	-	-
Unidentified total	≤ 0.5%	0	0	0	-	-	-	-	-	-	-
Total impurities	≤ 0.8%	0	0	0	-	-	-	-	-	-	-
Assay											
Trospium chloride	95.0% – 105.0%	98.0%	101.0%	98.6%	-	-	-	-	-	-	-
Microbiological quality	complies (Ph.Eur. 5.1.4, 3A)	complies	-	complies	-	-	-	-	-	-	-

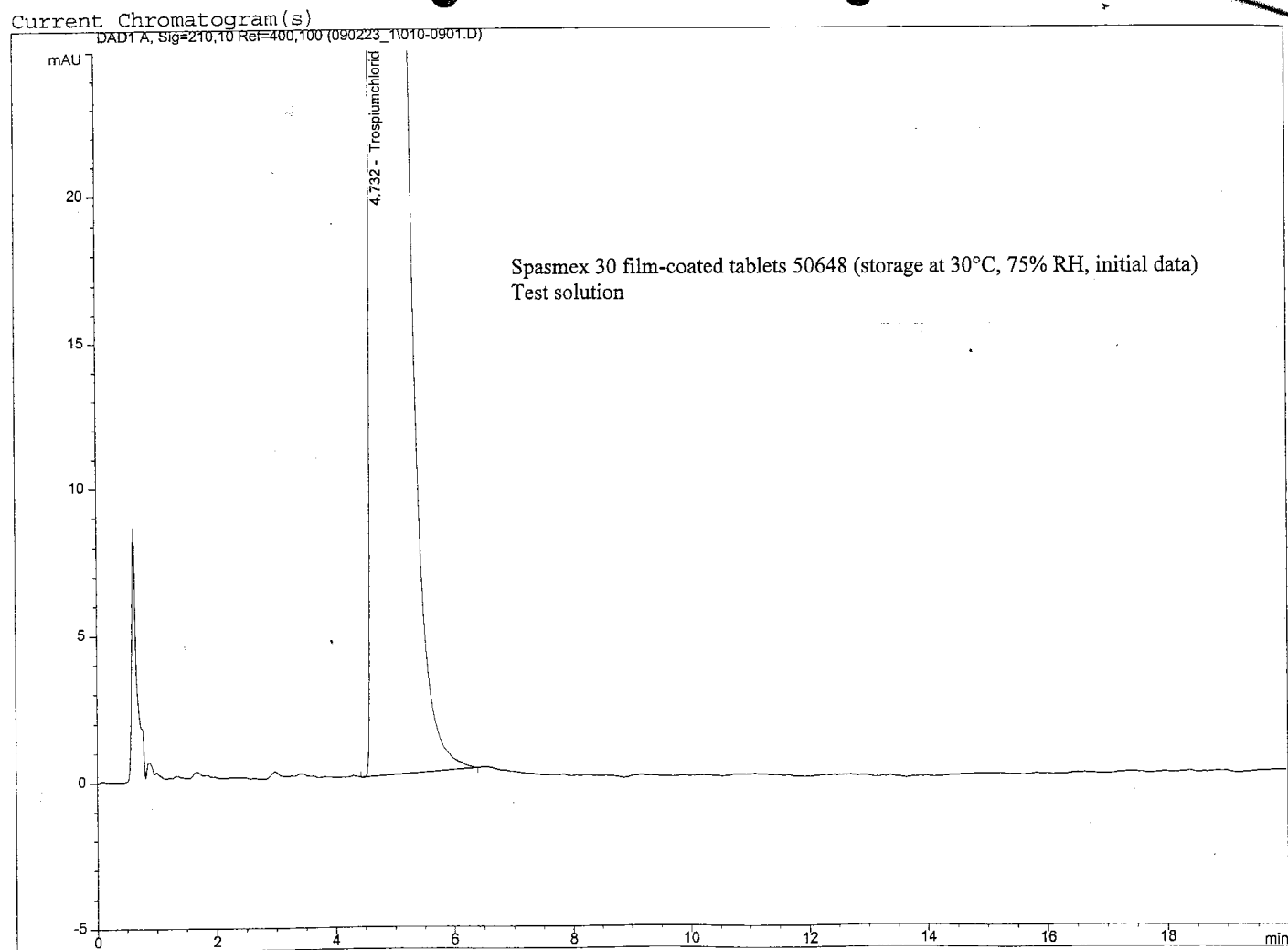
Print of window 38: Current Chromatogram(s)

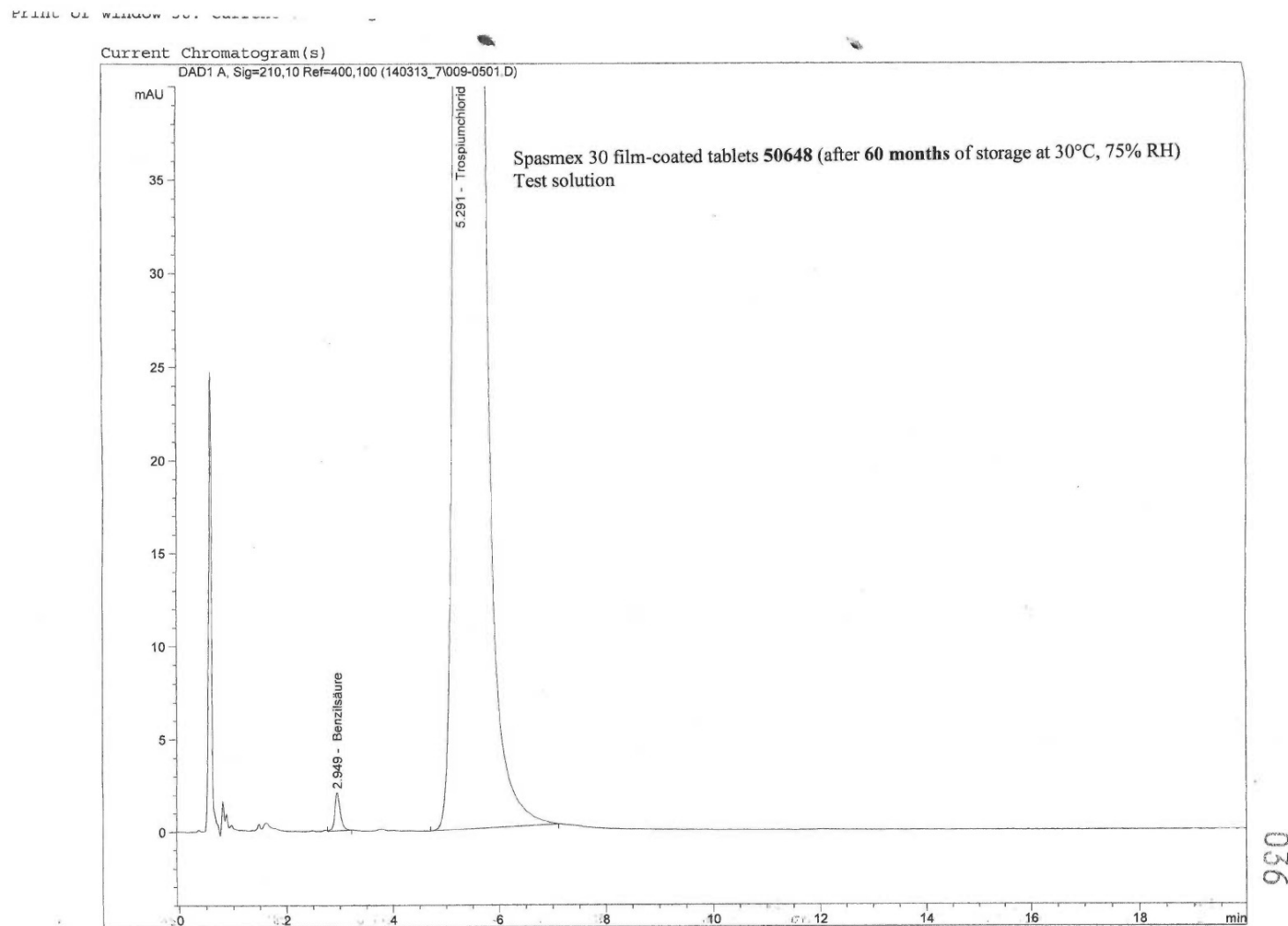


Trospium chloride 30 mg
Film-coated tablets

Module
3.2.P.8.3
Stability Data

Drug product	Trospium chloride 30 mg	Storage conditions		30°C ± 2°C, 75% ± 5% RH							
Dosage form	Film-coated tablets	Container closure system		Alu/PVC blister							
Manufacturer	Dr. R. Pflieger Chemische Fabrik GmbH	Date of storage		03.2009 (initial data evaluation: 02./03.2009)							
Batch number	50648										
Batch size	550 kg										
Date of manufacture	05.11.2008										
		MONTHS									
Test	Specification	0	3	6	9	12	18	24	36	48	60
Description	almost white, odourless film-coated tablets, round and biconvex, snap-tab score on one side, 9 mm in diameter	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Height	3.4 – 4.1 mm	3.8 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9mm	3.9mm	3.9 mm	3.9 mm	3.8 mm
Average mass	246.6 – 272.6 mg	258.7 mg	264.8 mg	265.8 mg	265.2 mg	264.2 mg	265.0mg	263.5mg	264.1 mg	265.2 mg	264.0 mg
Resistance to crushing	≥ 50 N	104 N	71 N	72 N	76 N	76 N	72 N	77 N	70 N	77 N	71 N
Disintegration	≤ 10 min	2' 44"	1' 27"	1' 20"	1' 30"	1' 20"	1' 13"	1' 24"	1' 22"	1' 30"	1' 13"
Subdivision	complies (Ph.Eur. Tablets)	complies	-	-	-	-	-	-			
Dissolution											
Trospium chloride	≥ 80% after 10 min	100.2%	99.3%	99.4%	97.7%	100.3%	101.9%	100.2%	99.1%	100.2%	98.7%
Identification											
Trospium chloride	positive (HPLC)	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Purity											
Benzilic acid	≤ 0.3%	not detect.	not detect.	< 0.1%	< 0.1%	< 0.1%	< 0.1%	< 0.1%	< 0.1%	< 0.1%	< 0.1%
Any unidentified	≤ 0.2%	not detect.	not detect.	not detect.	< 0.1%	not detect.	not detect.	not detect.	< 0.1%	not detect.	not detect.
Unidentified total	≤ 0.5%	0	0	0	0	0	0	0	0	0	0
Total impurities	≤ 0.8%	0	0	0	0	0	0	0	0	0	0
Assay											
Trospium chloride	95.0% – 105.0%	98.5%	101.6%	101.2%	101.8%	102.7%	100.8%	101.3%	102.3%	100.2%	99.7%
Microbiological quality	complies (Ph.Eur. 5.1.4, non-aqueous prep. for oral use)	complies	-	-	-	complies	-	-	complies	-	complies

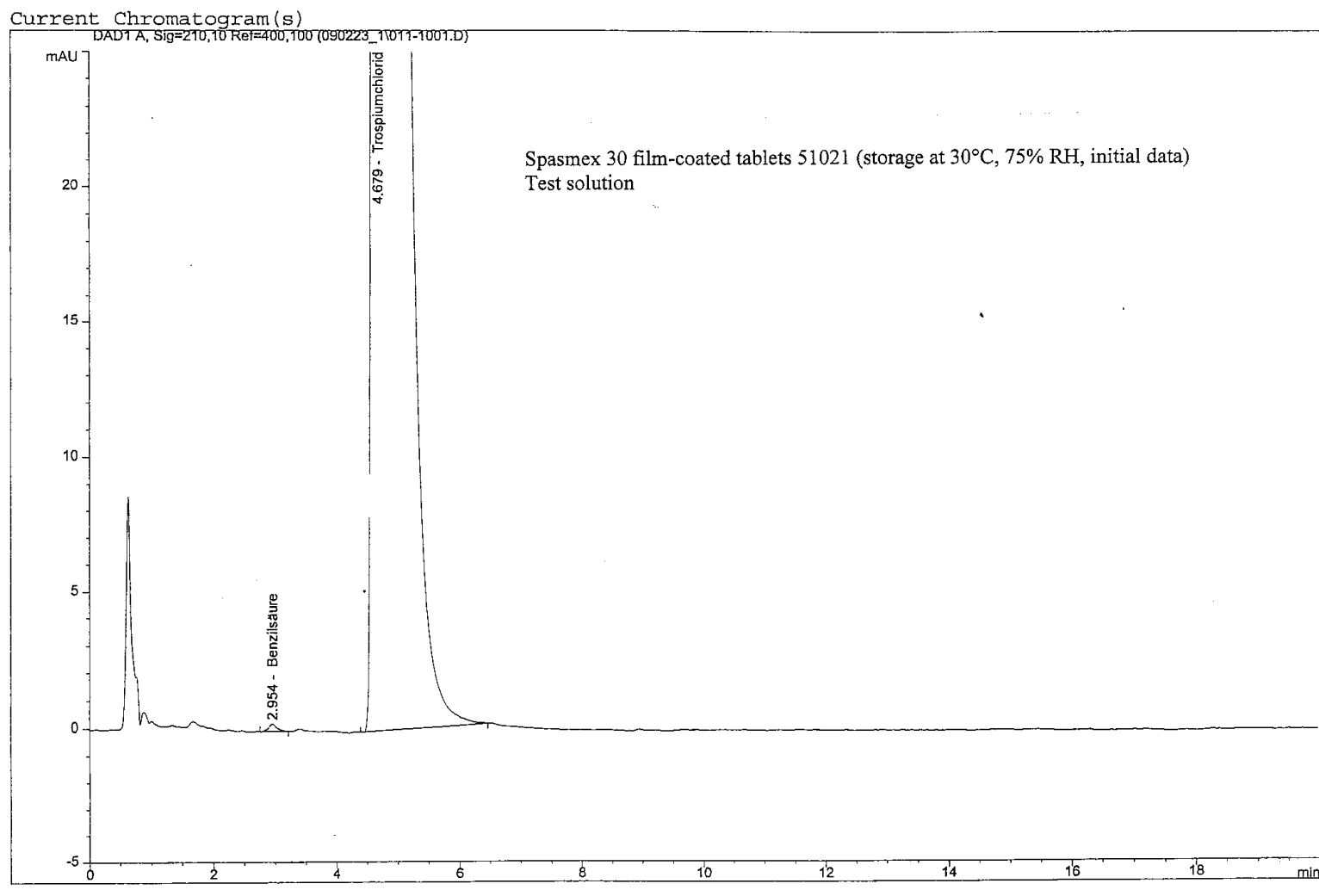


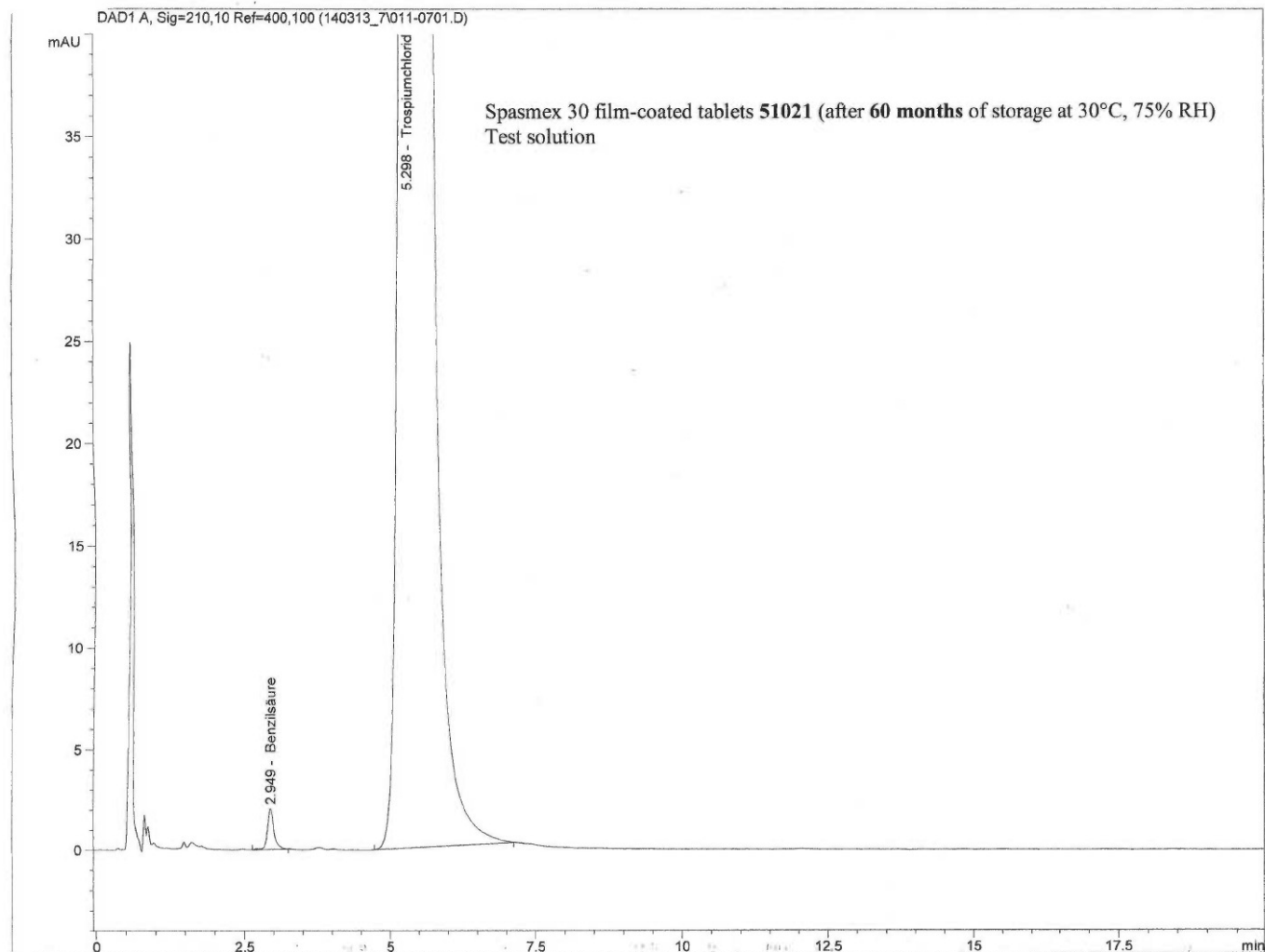


Trospium chloride 30 mg
Film-coated tablets

Module
3.2.P.8.3
Stability Data

Drug product	Trospium chloride 30 mg			Storage conditions		30°C ± 2°C, 75% ± 5 % RH					
Dosage form	Film-coated tablets			Container closure system		Alu/PVC blister					
Manufacturer	Dr. R. Pflieger Chemische Fabrik GmbH			Date of storage		03.2009 (initial data evaluation: 02./03.2009)					
Batch number	51021										
Batch size	550 kg										
Date of manufacture	05.12.2008										
		MONTHS									
Test	Specification	0	3	6	9	12	18	24	36	48	60
Description	almost white, odourless film-coated tablets, round and biconvex, snap-tab score on one side, 9 mm in diameter	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Height	3.4 – 4.1 mm	3.8 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm
Average mass	246.6 – 272.6 mg	258.2 mg	263.9 mg	263.9 mg	262.9 mg	262.6 mg	264.3mg	260.9mg	263.3 mg	263.8 mg	263.6 mg
Resistance to crushing	≥ 50 N	111 N	77 N	81 N	82 N	80 N	75 N	78 N	78 N	81 N	78 N
Disintegration	≤ 10 min	3' 42"	1' 43"	2' 07"	1' 34"	1' 34"	1' 30"	1' 40"	1' 29"	1' 48"	1' 33"
Subdivision	complies (Ph.Eur. Tablets)	complies	-	-	-	-	-	-			
Dissolution											
Trospium chloride	≥ 80% after 10 min	99.0%	98.9%	98.6%	99.1%	98.4%	100.0%	99.5%	98.5%	98.7%	99.9%
Identification											
Trospium chloride	positive (HPLC)	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Purity											
Benzilic acid	≤ 0.3%	≤ 0.1%	not detect.	< 0.1%	< 0.1%	< 0.1%	< 0.1%	< 0.1%	< 0.1%	< 0.1%	< 0.1%
Any unidentified	≤ 0.2%	not detect.	not detect.	not detect.	< 0.1%	not detect.	not detect.	not detect.	< 0.1%	not detect.	not detect.
Unidentified total	≤ 0.5%	0	0	0	0	0	0	0	0	0	0
Total impurities	≤ 0.8%	0	0	0	0	0	0	0	0	0	0
Assay											
Trospium chloride	95.0% – 105.0%	100.4%	102.0%	101.2%	102.4%	100.8%	100.9%	101.0%	99.1%	99.8%	100.2%
Microbiological quality	complies (Ph.Eur. 5.1.4, non-aqueous prep. for oral use)	complies	-	-	-	complies	-	-	complies	-	complies

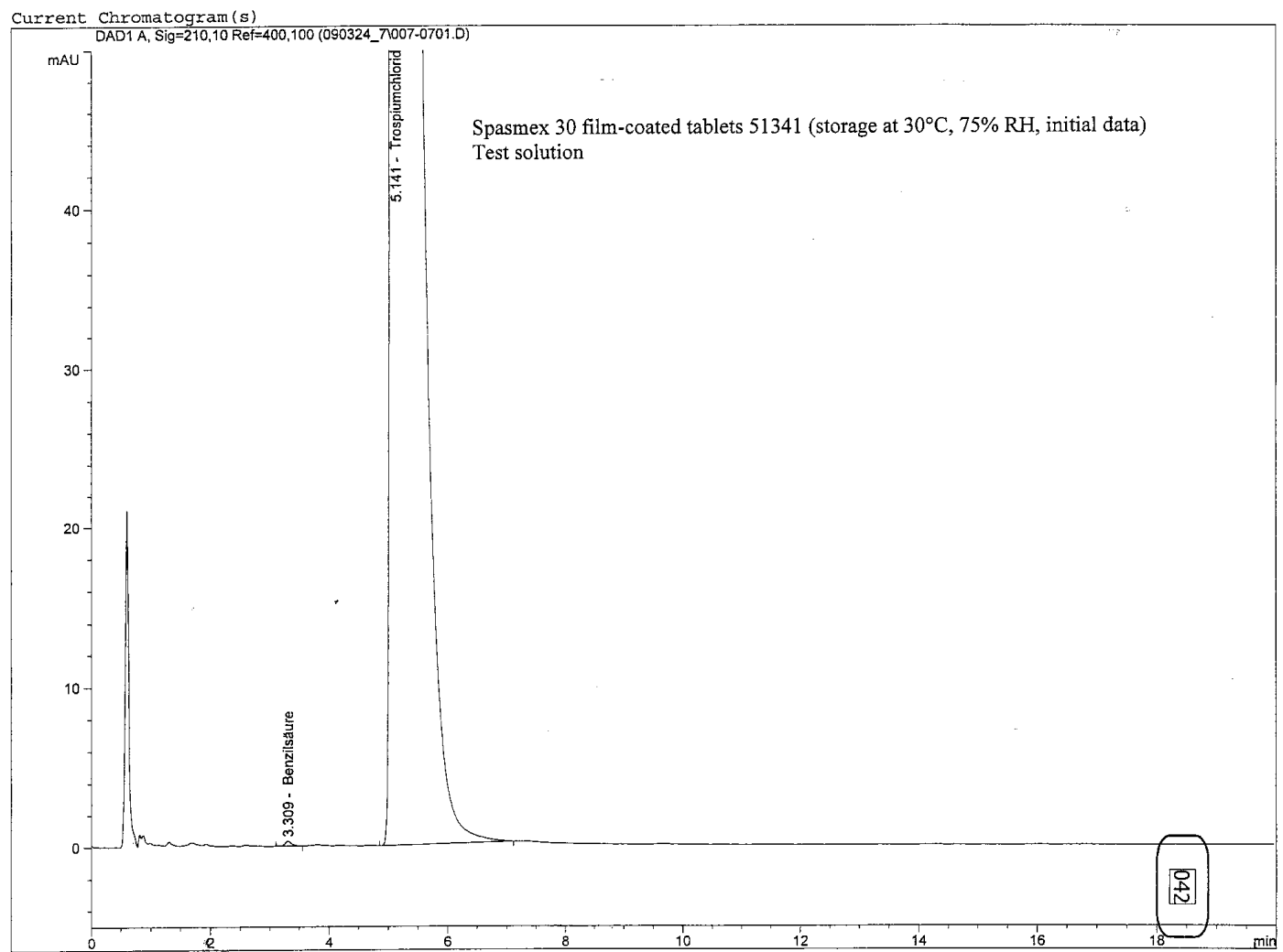




Trospium chloride 30 mg
Film-coated tablets

Module
3.2.P.8.3
Stability Data

Drug product	Trospium chloride 30 mg	Storage conditions		30°C ± 2°C, 75% ± 5% RH							
Dosage form	Film-coated tablets	Container closure system		Alu/PVC blister							
Manufacturer	Dr. R. Pflieger Chemische Fabrik GmbH	Date of storage		03.2009 (initial data evaluation: 02./03.2009)							
Batch number	51341										
Batch size	550 kg										
Date of manufacture	29.01.2009										
		MONTHS									
Test	Specification	0	3	6	9	12	18	24	36	48	60
Description	almost white, odourless film-coated tablets, round and biconvex, snap-tab score on one side, 9 mm in diameter	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Height	3.4 – 4.1 mm	3.8 mm	3.9 mm	3.9 mm	3.9 mm	3.9 mm	4.0 mm	4.0 mm	3.9 mm	3.9 mm	3.9 mm
Average mass	246.6 – 272.6 mg	258.8 mg	263.4 mg	263.1 mg	261.3 mg	263.2 mg	263.7mg	264.5mg	262.4 mg	262.0 mg	264.0 mg
Resistance to crushing	≥ 50 N	100 N	72 N	74 N	72 N	77 N	76 N	81 N	72 N	80 N	76 N
Disintegration	≤ 10 min	2' 31"	1' 32"	1' 18"	1' 48"	1' 33"	1' 32"	1' 27"	1' 24"	1' 48"	1' 24"
Subdivision	complies (Ph.Eur. Tablets)	complies	-	-	-	-	-	-			
Dissolution											
Trospium chloride	≥ 80% after 10 min	99.2%	100.5%	100.2%	98.4%	100.3%	100.9%	99.0%	98.4%	98.2%	100.6%
Identification											
Trospium chloride	positive (HPLC)	complies	complies	complies	complies	complies	complies	complies	complies	complies	complies
Purity											
Benzilic acid	≤ 0.3%	≤ 0.1%	not detect.	< 0.1%	< 0.1%	< 0.1%	< 0.1%	< 0.1%	< 0.1%	< 0.1%	< 0.1%
Any unidentified	≤ 0.2%	not detect.	not detect.	not detect.	< 0.1%	not detect.	not detect.	not detect.	< 0.1%	not detect.	not detect.
Unidentified total	≤ 0.5%	0	0	0	0	0	0	0	0	0	0
Total impurities	≤ 0.8%	0	0	0	0	0	0	0	0	0	0
Assay											
Trospium chloride	95.0% – 105.0%	99.5%	99.9%	100.9%	101.5%	100.6%	101.3%	102.4%	102.8%	98.5%	100.3%
Microbiological quality	complies (Ph.Eur. 5.1.4, non-aqueous prep. for oral use)	complies	-	-	-	complies	-	-	complies	-	complies



Print of window 38: Current Chromatogram(s)

