Potency comparison study between Rapid Labs CE and non-CE marked Blood Grouping Reagents compared with NIBSC Standards and Competitor CE marked reagents

The quality of blood grouping reagents is clearly an important factor for safe blood transfusion. The NIBSC (National Institute for Biological Standards and Control) are a global institution that ensures the quality of biological products through biological materials and carrying out research.

Rapid Labs manufacture and supply a range of CE and non-CE marked blood grouping reagents to over 100 countries. CE marking is the medical device manufacturer's claim that a product meets the essential requirements of all relevant European Medical Device Directives. The Directives outline the safety and performance requirements for medical devices in the European Union (EU). The CE mark is a legal requirement to place a device on the market in the EU. CE-marked products typically have a higher cost than non-CE marked versions due to the high regulatory cost of achieving and maintaining CE registration.

For customers outside the EU that do not require CE-marked medical devices, Rapid Labs non-CE marked blood grouping reagents are an affordable alternative. Where possible, these reagents have been developed with a higher titre than our CE-marked versions, allowing them to withstand the rigours of long-haul shipping in higher temperatures (providing they are refrigerated at 2-8°C immediately upon arrival).

We compared the potency between our CE-marked and non-CE marked anti-A, anti-B and anti-D blood grouping reagents, along with another manufacturer of CE-marked blood grouping reagents against the NIBSC standards. Performance evaluation was undertaken in accordance with BS EN 13612:2002 Performance Evaluation of *In Vitro* Diagnostic Medical Devices.

In this article, we shall demonstrate how both Rapid Labs CE and non-CE ranges passed or exceeded the NIBSC standards for potency - even when used at maximum shelf life.

Reagents Tested

- NIBSC anti-A lyophilized reagent (03/188), reconstituted with 1ml deionized water and diluted 1:8 with buffered saline to reach the minimum acceptable potency[1].
- NIBSC anti-B lyophilized reagent (03/164), reconstituted with 1ml deionized water and diluted 1:4 with buffered saline to reach the minimum acceptable potency[1].
- NIBSC anti-D lyophilized reagent (99/836), reconstituted with 1ml deionized water and diluted 1:3 with buffered saline to reach the minimum acceptable potency[1].

- Rapid Labs CE-marked anti-A (BC-A)
- Rapid Labs CE-marked anti-B (BC-B)
- Rapid Labs CE-marked anti-D (BC-D)

- Rapid Labs anti-A (BG-A)
- Rapid Labs anti-B (BG-B)
- Rapid Labs anti-D (BG-D)

- Competitor CE-marked anti-A Reagent
- Competitor CE-marked anti-B Reagent
- Competitor CE-marked anti-D Reagent

Method

Each reagent was aliquoted into 12 tubes with doubling dilution as recommended by the Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee[2] (1:1, 1:2, 1:4, 1:8, 1:16, 1:32, 1:64, 1:128, 1:256, 1:512, 1:1024 and 1:2048). 2-3% suspension of A1rr, A2rr, Brr and B1r blood cells, supplied by the NHSBT (lot no. 3301, expiry 15/04/2019) was added to each tube for their respective reagents. The tubes were then centrifuged for 1 minute at 1000rpm and resuspended by gentle agitation. The potency for each dilution was graded according to the Grading System for Serological Tests (as defined by the Guidelines for the Blood Transfusion Services in the United Kingdom, 2013)[3]:

Reaction grade	Description
Grade 5	Cell button remains in one clump or dislodges into a few large clumps
Grade 4	Cell button dislodges into numerous large clumps
Grade 3	Cell button dislodges into many small clumps
Grade 2	Cell button dislodges into finely granular but definite, small clumps
Grade 1	Cell button dislodges into fine granules
Grade 0	Negative result
Unless otherwise stated, an unequivocal manual tube reaction is defined as a grade 3 or greater and for column tests as 2+ or greater	

Results

The potency grades for each reagent are shown below:

anti-A Blood Grouping Reagents

Dilution Factor	1	2	4	8	16	32	64	128	256	512	1024	2048	Total Score (/60)
NIBSC Score	5	5	5	5	5	5	4	3	2	1	1	1	42
Rapid Labs (CE) Score	5	5	5	5	5	5	5	4	4	3	2	1	49
Rapid Labs (non-CE) Score	5	5	5	5	5	5	5	5	5	3	3	3	54
Competitor A (CE) Score	5	5	5	5	5	5	4	3	3	2	1	1	44

As defined by the JPAC Transfusion guidelines[3], agglutination should be demonstrated at a 1:8 dilution, with a minimum accepted total potency score of 40. All blood grouping reagents passed, with the Rapid Labs non-CE marked reagent scoring the highest level of potency.

anti-B Blood Grouping Reagents

Dilution Factor	1	2	4	8	16	32	64	128	256	512	1024	2048	Total Score (/60)
NIBSC Score	5	5	5	4	4	3	2	1	1	0	0	0	30
Rapid Labs (CE) Score	5	5	5	5	5	4	4	3	3	2	1	1	43
Rapid Labs (non-CE) Score	5	5	5	5	5	5	5	4	3	2	1	0	45
Competitor A (CE) Score	5	5	5	5	4	3	3	3	2	1	1	1	38

As defined by the JPAC Transfusion guidelines[3], agglutination should be visible at a 1:4 dilution, with a minimum accepted total potency score of 30. All reagents passed, with the Rapid Labs non-CE marked reagent scoring the highest level of potency.

anti-D Blood Grouping Reagents

Dilution Factor	1	2	4	8	16	32	64	128	256	512	1024	2048	Total Score (/60)
NIBSC Score	5	4	4	3	2	2	1	1	0	0	0	0	22
Rapid Labs (CE) Score	5	5	4	4	4	3	3	3	2	2	2	1	38
Rapid Labs (non-CE) Score	5	5	4	4	4	3	2	2	1	1	0	0	31
Competitor A (CE) Score	5	5	4	3	3	3	2	1	1	1	1	1	30

As defined by the JPAC Transfusion guidelines[3], agglutination should be visible at a 1:3 dilution, with a minimum accepted total potency score of 20. All reagents passed, with the Rapid Labs CE-marked reagent scoring the highest level of potency.

Further Potency Evaluation using Rapid Labs reagents close to expiry/recently expired:

Rapid Labs non-CE marked blood groups are offered in regions where CE registration is not a requirement and are a more affordable option.

Further testing was completed using expired/approaching expired Rapid Labs non-CE marked blood grouping reagents to investigate how potency changes over time using the same NHSBT red cells from the initial comparison study. The overall scores were compared to the freshly reconstituted NIBSC reagent to see if the potency of these expired/close to expired reagents remained within the NIBSC standards:

Anti-A Potency Results (< 1 month shelf life remaining, Lot # A0417-11, exp 04-2019)

Dilution Factor	1	2	4	8	16	32	64	128	256	512	Total Score (/60)
Rapid Labs (non-CE) Score	5	5	5	5	5	5	5	5	4	3	47

Anti-B Potency Results (< 1 month shelf life remaining, Lot # B0417-11A, exp 04-2019)

Dilution Factor	1	2	4	8	16	32	64	128	256	512	Total Score (/60)
Rapid Labs (non-CE) Score	5	5	5	5	5	5	5	4	3	3	45

Anti-D Potency Results (< 1 month shelf life remaining, Lot # D0417-11C, exp 04-2019)

Dilution Factor	1	2	4	8	16	32	64	128	256	512	Total Score (/60)
Rapid Labs (non-CE) Score	5	5	4	4	4	3	2	2	1	1	31

Anti-D Potency Results (Expired > 2 months, Lot # D0117-25B, exp 01-2019)

Dilution Factor	1	2	4	8	16	32	64	128	256	512	Total Score (/60)
Rapid Labs (non-CE) Score	5	4	4	3	2	1	1	1	1	1	23

Conclusion

All Rapid Labs CE-marked and non-CE marked anti-A, anti-B and anti-D blood grouping reagents exceeded the potency of the NIBSC standards. Our non-CE marked anti-A, anti-B and anti-D reagents have also shown to meet or exceed the NIBSC standards when used at their maximum shelf life, demonstrating a high level of stability. This study demonstrates that our non-CE marked blood grouping reagents offer an affordable and effective solution for countries that do not require CE-registered products, whilst ensuring they meet the industry standard of potency.

References

1.WHO International Standard: Minimum Potency of Anti-A and Anti-B Blood Grouping Reagents NIBSC code: 03/188 & 03/164 Instructions for Use (2008): Version 3.

2.Recommended serological techniques for reagent testing. Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee: https://www.transfusionguidelines.org/red-book/chapter-11-reagent-manufacture/11-4-recommended-serological-techniques-for-reagent-testing

3. Specifications, performance evaluation and quality control of blood grouping reagents. Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee: https://www.transfusionguidelines.org/red-book/chapter-11-reagent-manufacture/11-2-specifications-performance-evaluation-and-quality-control-of-blood-grouping-reagents